PRICE'S TEXTBOOK
OF THE
PRACTICE OF MEDICINE

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PRICE'S TEXTBOOK
OF THE
PRACTICE OF MEDICINE

BY VARIOUS AUTHORS

EDITED BY
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PREFACE TO NINTH EDITION

After thirty three years in which he devoted himself to his Textbook Dr Frederick W Price has resigned the editorship to another The new editor and all the contributors wish to express their sympathy for him in his recent long and serious illness and their wish that good health and happiness may be restored to him in his retirement We hope that we have succeeded in making the new edition worthy of British medicine and of Dr Price

The purpose and scope of the book remain the same as when it was originally conceived namely the presentation of a comprehensive survey of the practice of modern medicine in the form of a textbook each subject being dealt with in an essentially practical manner prominence being given to diagnosis prognosis and treatment It is our hope that the book will be of service alike to clinical teachers, physicians general practitioners and students

Since the last edition appeared we have to record with deep regret the death of our colleagues Dr Charles R Box Dr Geoffrey Evans Dr A F Gow Lord Horder Professor R H A Plimmer and Mr Charles Donald whom we looked forward to welcoming here as a new contributor Mr Donald had completed his articles on Acute Intestinal Obstruction Appendicitis and Acute Peritonitis and they appear in the present edition We feel that they are a better monument to his accomplishments and to his untimely death than any words of ours

We wish to thank the many contributors to earlier editions who very generously wrote to say that they thought current teaching and opinion in our medical schools could be expressed better by younger men with charge of beds in our teaching hospitals Accordingly many new names appear in the list of contributors and we extend a most cordial welcome to Dr F R Boland Dr R R Bomford Dr Wallace Brigden Professor R B Hunter Mr Ambrose King Professor B G Maegraith Dr Brian Russell Dr G A Smart and Professor Clifford Wilson

It is a pleasure to state our indebtedness to a number of colleagues who have helped us in making the new edition We are especially grateful to Dr Lirian Williams upon whom the work of checking the proofs has mainly fallen His devotion to this arduous task was equalled only by that of Mr A E Gray of the Oxford University Press who not only shared the burden of correcting the proofs but also compiled the entire index For the courage patience and kindness with which they have carried out their secretarial duties it is a pleasure to thank Miss Helen Michie Miss Jean Player and Miss Naomi Wright To our distinguished contributors who have lavished their time and their learning in producing this unique compilation of modern knowledge we wish to express our warmest gratitude and appreciation For a great deal of help cordially given and also for much forbearance we have to thank our publishers and printers

DONALD HUNTER

WHITECHAPEL E I
April 1956

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INTRODUCTION

HEART disease is by far the most common cause of natural death in civilised communities in the more temperate zones of the world It is responsible for at least two fifths of all such deaths and for an annual mortality rate in the general population of about 0 45 per cent Both incidence and mortality curves have been rising steadily for many years a fact which is not fully explained by ageing populations and by the control of infectious fevers pulmonary tuberculosis and pyogenic infections The incidence and mortality of cancer for example show no comparable increase Ischæmic heart disease particularly is becoming more frequent

It is by no means easy to estimate the prevalence of each kind of heart disease for selection plays havoc with most personal and hospital statistics whilst random samples usually suffer from inaccurate diagnosis For example amongst a consecutive series of 10 000 cases of cardiovascular disease that I have seen personally during the last few years 900 or 9 per cent had congenital heart disease which is about six times the number that would be expected in a random sample of cardiovascular cases The other side of the picture is illustrated by the Registrar General s statistical review for 1953 in which the chief cause of all deaths is myocardial degeneration a diagnosis which is not recognised in cardiovascular clinics whilst cor pulmonale is not mentioned at all Nevertheless an attempt has been made to assess the prevalence of the more important forms of heart disease based on the literature my own data and the Registrar General s statistical reviews A few general observations may be made first

The population of England and Wales in 1953 was approximately 44 000 000 There were 503 529 deaths during this year Of these 183 917 were due to heart disease 68 069 to a cerebral vascular accident and 30 392 to bronchitis and emphysema At least half of all the deaths were therefore cardiovascular and over half if cor pulmonale had been included For comparison there were 89 680 deaths from neoplasm (of which 15 132 were due to carcinoma of the lung) 20 759 from pneumonia and 8 902 from tuberculosis

The ensuing table is no more than an approximate estimate of the incidence of the more important kinds of heart disease and the many blanks represent lack of reliable information

INCIDENCE OF CHIEF FORMS OF HEART DISEASE

	PERCENTAGE OF CLINICAL CASES OF HEART DISEASE	PERCENTAGE OF POPULATION	PERCENTAGE OF CARDIAC DEATH	PERCENTAGE OF ALL DEATHS
Bacterial endocarditis	1 0	—	0 17	0 07
Congenital heart disease (surviving infancy)	1 5	0 1	0 9	0 36
Cor pulmonale	5 0	—	5–15	2–6
Dissecting aneurysm	0 [illegible]	—	0 45	0 18
Hyperkinetic circulatory states	0 3	—	—	—
Hypertension	25 0	3 0	10 0	4 0
— cerebral vascular accidents	—	—	—	13 5
Ischæmic heart disease	30 0	[illegible] 0	31 [illegible]	12 5
Miscellaneous and uncertain	6 5	—	—	—
— degenerative	—	—	35 0	14 0
Myocarditis and other rare or obscure cardiopathies	0 3	—	—	—
Pericarditis (primary)	1 0	—	—	—
Pulmonary embolism	—	—	6 5	2 6
Pulmonary hypertension (primary or thrombo embolic)	0 [illegible]	—	—	—
Rheumatic carditis	5 0	0 5	0 15	0 06
Rheumatic heart disease (chronic)	1[illegible] 0	1 5	4 5	1 8
Rhythm changes—primary	[illegible] 0	—	—	—
Syphilitic aortitis	1 0	—	0 5	0 2
Thyrotoxic heart disease	[illegible] 0	—	0 [illegible]	0 08

CHAPTER I

THE CHIEF SYMPTOMS OF HEART DISEASE

HISTORY TAKING

TO take an accurate and relevant history is one of the most difficult and important arts in medicine Sometimes a complete diagnosis can be made from the history alone and not infrequently the possibilities can be whittled down to two or three A good history should at least indicate the system involved or it should point unerringly to some group or groups of diseases A common mistake is the failure to analyse any given symptom sufficiently in cardiovascular work this applies especially to pain breathlessness palpitations and syncope The student is usually taught to encourage the patient to tell his story in his own words and to record them more or less verbatim Yet such an account may be verbose irrelevant inaccurate and misleading It is an axiom that the leading question must be avoided at all cost yet again an experienced physician must know that the ability to put the appropriate leading question at the right moment and the intelligent interpretation of its reply are invaluable It is not pretended that leading questions may not lead to false information if the power of their suggestion is not appreciated by the questioner and it is agreed that much may be lost by failure to allow the patient freedom and time to express his complaints in his own way but the average patient will not mention half the available information until he is pressed and the data freely given must be checked as at the bar For example in the differential diagnosis between a neural and non neural somatic lesion an accurate description of the quality of the pain may determine the issue immediately yet the majority of patients will volunteer no information concerning the quality of pain and if asked to describe it will do so inadequately They may say it is aching or sharp but fail to enlarge on this even when urged to do so In answer to the leading question Does it tingle? however they may reply at once in the affirmative It is essential to realise that the matter does not end there that such a positive reply to a leading question demands the most penetrating cross examination until the questioner is satisfied that the pain really does tingle and that the patient is not merely saying so because it seems the easier answer It is scarcely too much to say that the best history taker is he who can best interpret the answer to a leading question Appropriate leading questions can only be asked however when the proffered history has provided sufficient data upon which to work and if the physician has sufficient knowledge of the possibilities then entailed It is this latter factor which makes it easier for the expert than for the student

SYMPTOMS

The symptoms of heart disease vary considerably according to the nature of the cardiopathy and the kind of physiological disturbance in the circulation that results each will be discussed in particular relation to the form of heart disease in which it occurs in subsequent chapters, but it may help here to survey the subject in general

To begin with it should be thoroughly understood that cardiovascular disease may be severe without any symptoms whatever good examples of this axiom are coarctation of the aorta pulmonary stenosis atrial septal defect aortic stenosis malignant hypertension primary pulmonary hypertension and aortic aneurysm even cardiac infarction may be silent

A second point of general interest is that patients rarely appreciate what is a heart symptom and what is not The most classical example of this is the well known paradox that patients with angina pectoris (including doctors) often complain of indigestion whereas those with dyspepsia or left inframammary pain may be convinced that their hearts are at fault Headaches and dizziness are frequently attributed to high blood pressure when there is no hypertension palpitations which are usually innocent, are a common source of anxiety fatigue and lack of energy resulting from psychological conflict are often ascribed to failing circulation On the other hand breathlessness due to mitral stenosis or left ventricular failure may be attributed to bronchitis, an attack of paroxysmal cardiac dyspnœa to bronchial asthma and coughing from pulmonary venous congestion to over smoking A man with gross congestive heart failure has even been known to present himself first at a skin clinic on account of pruritis (due to jaundice)

Finally after recording the symptoms faithfully in chronological order the absence of any important symptom that might reasonably have been expected under the clinical circumstances should also be noted In a case presenting with mitral stenosis for example with effort breathlessness of moderate grade as the only positive symptom, an experienced physician would record the absence of hæmoptysis winter bronchitis orthopnœa paroxysmal *cardiac dyspnœa angina pectoris, recurrent palpitations* peripheral embolism and œdema because all these are important symptoms of mitral stenosis each having its own particular meaning On the other hand he would not record the absence of syncope squatting transient cyanosis headache heat intolerance Raynaud s phenomenon and a host of other negatives which under the clinical circumstances are irrelevant The recording of a negative implies that the appropriate leading question has been asked

PAIN

Cardiac pain is ischæmic being due to stimulation of afferent nerve endings in the myocardium by metabolites resulting from oxygen deficiency in working muscle

The commonest cause is occlusive coronary atherosclerosis In *simple angina pectoris* the coronary flow is adequate at rest but becomes inadequate when the demands of the myocardium are increased by exercise In *acute coronary insufficiency* the flow suddenly becomes inadequate at rest usually as a result of thrombosis but is still sufficient to prevent necrosis In *acute cardiac infarction* failure of the coronary flow to part of the heart muscle leads to ischæmic necrosis (gangrene)

Pain in angina pectoris is characteristically central in position pressing in quality brief in duration and closely related to effort It is felt more across the chest than in the mid line and may radiate to the shoulders down both arms into the neck or jaws and through to the back It is usually described as heavy or squeezing but may be bursting burning or like indigestion It occurs especially on walking particularly after meals on a cold day against the wind or uphill It forces the patient to stop or slow down and disappears in two or three minutes when he stands still In acute coronary insufficiency the pain also occurs at rest lasts longer and is often more severe and in cardiac infarction it continues for hours, even for a day or two

The chief cause of a sudden increase in the frequency or duration of cardiac pain is coronary thrombosis whether it leads to cardiac infarction or not Coronary occlusion due to subintimal hæmorrhage is rare Diabetes mellitus myxœdema, xanthomatosis and familial or idiopathic hyper cholesterolæmia are often complicated by angina because they encourage atherogenesis Thromboangiitis obliternans polycythæmia vera, shock and trauma may be complicated by cardiac infarction because they encourage coronary thrombosis Infarction secondary to subintimal hæmorrhage may be caused by injury to the chest or too vigorous anticoagulant therapy

Angina may also be caused by any condition which adversely disturbs the balance between cardiac work and coronary blood flow There are four classical examples (1) severe hypertension may cause angina when the coronary arteries are normal because the work of the heart is increased by the high peripheral resistance (2) any of the hyperkinetic circulatory states such as thyrotoxicosis may encourage angina by increasing cardiac work in respect of the volume pumped (3) angina in syphilitic aortitis is due to reduction of coronary flow owing to obstruction at the mouths of the coronary arteries, (4) angina during a paroxysmal rhythm change with rapid ventricular rate is due to the poor coronary flow that results from the shortened periods of diastole

In the presence of healthy coronary arteries physiological work and normal coronary flow angina may yet occur if the oxygen supply is deficient This is the chief cause of cardiac pain in severe anæmia although extra work due to a raised cardiac output is contributory Angina similarly pro voked might be expected in anoxic cor pulmonale but it is uncommon and when present may well be due to coincidental coronary disease Angina rarely occurs from anoxia in cyanotic congenital heart disease Finally

mechanical obstruction to the circulation may cause angina by strictly limiting the cardiac output and hence the coronary flow while increasing the work of the heart Examples include aortic stenosis mitral valve disease, pulmonary hypertension massive pulmonary embolism and pulmonary stenosis

Pericardial pain is usually sharper more left sided than central and may be referred to the neck or flank It is relatively long lasting and independent of effort

Pain from *aneurysm of the aorta* is usually due to pressure erosion and from *dissecting aneurysm* to a variety of causes including stripping of the adventitia involvement of the segmental arteries coronary occlusion and hæmopericardium

Despite the characteristic nature and behaviour of cardiac pain the vast majority of lay persons believe it is situated in the region of the left breast *Innocent left inframammary pain* is therefore one of the commonest symptoms that brings a patient to seek medical advice This pain is a long lasting dull ache momentarily accentuated from time to time by sudden sharp jabs it is situated well to the left bears no direct relationship to effort may prevent the patient lying on the left side and is often associated with superficial tenderness Thus it differs radically from angina pectoris in site quality duration and behaviour, i e in all four major characteristics

Other varieties of chest pain which may have to be distinguished from angina pectoris include pain referred from the spine œsophagus stomach duodenum gall bladder and mediastinum and local pain arising from structures in the chest wall such as muscles and ligaments

DYSPNŒA

Breathlessness is the most common and perhaps the most important of all symptoms relating to heart disease and also the most complex The physiology of cardiac dyspnœa is discussed more fully in the chapters on special techniques (respiratory function) heart failure and mitral stenosis

Shortness of breath like all other symptoms is subjective and the intensity of the sensation depends in no small measure on the patient s acuteness of perception Individual variation is great and explains why under exactly similar physiological circumstances one patient appears to be incapacitated while another carries on his normal occupation with relative tranquillity

Hysterical dyspnœa or hyperventilation is rather different for here the added stimulus to breathe is purely cortical and the activity may continue in the presence of true alkalæmia and oxygen supersaturation A similar situation may occur in encephalitis Hyperventilation may also be caused by various proprioceptive impulses such as pain and especially from activity of voluntary muscle as on exercise (Comroe and Schmidt 1943)

The simplest form of dyspnœa is suffocation The intense desire for breath is due to direct stimulation of the respiratory centre by a *rising*

carbon dioxide tension (Haldane and Priestley 1905) and reflex stimulation from *arterial hypoxia* acting on chemoreceptors in the carotid and aortic bodies (Heymans *et al*, 1939) Breathlessness of this kind occurs in asphyxia from any cause e g drowning strangulation peripheral respiratory paralysis tracheal obstruction, severe bronchial asthma advanced emphysema bilateral pneumothorax and acute pulmonary œdema *The fault lies with ventilation* an insufficient number of alveolæ are filled with fresh air at each breath

A second easily understood form of dyspnœa results from *breathing ill conditioned air* i e air with too low an oxygen content or too high a carbon dioxide content Ventilation is normal but the gases are at fault

A third form is encountered in diabetic acidosis and uræmia Here both ventilation and inhaled gases are normal but *the arterial pH is low* and it is this which excites the chemoreceptors

Hypoxia may result from *structural change in the alveolar walls* so that proper interchange of oxygen between alveolar air and pulmonary capillary blood is hindered This may occur when there is widespread interstitial fibrosis of the lung

Hypoxic dyspnœa associated with hyperventilation also occurs in cases of *right to left intracardiac shunt* as in Fallot s tetralogy

A sixth major cause of dyspnœa is severe anæmia when there is *insufficient hæmoglobin* to carry the oxygen

Rapid shallow breathing may result from *hyperactivity of the reflex described by Hering and Breuer* (1868) whereby relatively little inflation of the lungs arrests inspiration this is the type of dyspnœa seen in pneumonia

None of the above mentioned mechanisms accounts for ordinary cardiac dyspnœa In left ventricular failure and mitral stenosis dyspnœa is closely related to pulmonary venous congestion both arterial oxygen and carbon dioxide content are normal and the cardiac output at rest is not necessarily reduced The difficulty in breathing is attributed to *greater resistance on the part of the turgid lungs to both inflation and deflation* so that the muscles of respiration have to work harder a higher negative intrathoracic pressure is required for inspiration and even a slight positive pressure may be necessary for expiration (Christie and Meakins 1934)

In heart failure without pulmonary venous congestion from primary pulmonary hypertension or pulmonary stenosis for example dyspnœa is far less pronounced but it is still present and requires a different explanation The cardiac output is lower in these cases and the arterio venous oxygen difference higher so that increased ventilation may be necessary to ensure full oxygenation of the grossly unsaturated blood arriving in the lungs This hyperventilation may be chemically induced by *tissue hypoxia resulting from the low cardiac output* (Gesell 1925)

Special varieties of dyspnœa known as orthopnœa paroxysmal cardiac dyspnœa cardiac asthma and Cheyne Stokes breathing are fully discussed in the section on heart failure (Chapter VII)

ŒDEMA

When due to heart disease œdema is a sign of failure It is attributed to sodium retention as explained in Chapter VI and in a sense therefore is renal in origin In the majority of cases it is associated with a low cardiac output and a raised venous pressure The latter is due partly to eleva tion of the right ventricular end diastolic pressure and partly to the hydræmia resulting from sodium retention it is not itself responsible for the dropsy

There are many causes of œdema other than heart failure and although most of them are well known serious errors in etiological diagnosis are still all too common A brief review of the subject will not therefore be out of place here

Physiologically it is thought that water, electrolytes and certain other small molecules such as sugar and urea, leave the blood stream at the arterial end of the capillaries and re enter at the venous end the forces at work including the hydrostatic and osmotic pressures within and without the vessels and the permeability of the vascular endothelium At the arterial end of the capillary the hydrostatic pressure exceeds the osmotic at the venous end it is the other way about Thus the hydrostatic pressure on the arterial side of a capillary loop averages about 31 mm Hg and on the venous side about 12 mm Hg (Landis 1929) the tissue pressure outside the wall of the capillary is only 2 or 3 mm Hg (Burch and Sodeman 1937) and the effective colloid osmotic pressure of the plasma is usually said to be about 25 mm Hg It has been calculated by Krogh (1929) that the total capillary filtering surface in man is about 6 300 square metres The normal state of fluid balance may be upset in favour of the tissues by raising the hydrostatic pressure within the capillaries or reducing it without by reducing the osmotic pressure within the capillaries or raising it without or by increasing the permeability of the vascular endothelium (Starling 1895–6)

Increased hydrostatic pressure at the venous end of the capillaries is the cause of *œdema in venous thrombosis* cirrhosis of the liver with tense ascites and in partial or complete *obstruction of the superior or inferior vena cava* Low extra capillary pressure may determine the site of œdema but does not cause it Lax tissue occurs naturally in certain situations e g in the infraorbital region and may be demonstrated subcutaneodsly following considerable loss of weight or when the skin has been stretched by previous dropsy Reduction of capillary osmotic pressure is due mainly to reduction of plasma albumin Œdema usually develops when the total blood proteins fall below 5 G per cent *Nephrosis protein starvation severe chronic anæmia* and *gross protein loss* in pleural or peritoneal exudates may provide examples of such œdema The chief effect of increasing the permeability of the capillaries is to allow more albumin to escape into the tissue spaces (a certain amount escapes normally and re enters the blood stream via the lymphatics) and so to increase the osmotic pressure of the tissue fluid

Œdema with a high protein content (3 to 4 G per cent) results Such œdema may be associated with *burns, trench feet insect bites* and *allergy* (e g Quincke s disease) *Lymphatic œdema* has a similar high protein content but is also rich in cholesterol (White and Sachs 1950)

Œdema due to *sodium and water retention* is associated with hydræmia This raises the hydrostatic filtering pressure of the capillaries and lowers the osmotic pressure Physiologically, the amount of water retained or excreted is controlled by the hypothalmus via the neurohypophysis osmo receptors in the hypothalmus react to dilution of the plasma by inhibiting the liberation of anti diuretic hormone by the neurohypophysis so that diuresis results on the other hand if the plasma becomes more concentrated an increased quantity of anti diuretic hormone is liberated and the flow of urine is suppressed (Verney 1946) Physiological hydræmia sometimes accompanied by slight œdema occurs during the *premenstrual phase* in women (Frank 1931) and has been attributed to elevation of the œstradiol progesterone ratio (Greene and Dalton 1953) This also may act by stimulating the liberation of anti diuretic hormone

Famine œdema is complex It may be associated with thiamine deficiency (wet beri beri) or with serious reduction of plasma proteins (Denz 1947) but in other cases neither of these factors can be held responsible this last group is characterised by diuresis in the horizontal position and with enlargement of the adrenal glands (Sinclair 1948)

Renal œdema is discussed in Chapter VI

In practice the causes of œdema most often confused with cardiac œdema are Milroy s lymphatic deficiency, premenstrual hydræmia bilateral phlebo thrombosis and chronic nephritis

FATIGUE

Since fatigue cannot be seen like laboured breathing or œdema it is apt to be underestimated as a symptom of heart failure yet it is as closely related to a low cardiac output as dyspnœa is to pulmonary venous con gestion Thus patients with tight mitral stenosis and a low pulmonary vascular resistance complain of dyspnœa for the chief physiological result of the situation is pulmonary venous congestion but if the pulmonary vascular resistance is extreme congestion of the lungs is relieved at the expense of right ventricular failure and a low cardiac output, and dyspnœa is replaced by fatigue

Patients complain of heaviness of the limbs on exertion weakness or lack of vigour or general tiredness and exhaustion The physiology of such fatigue is too complex and ill understood to discuss here with profit The practical problem is to distinguish cardiac fatigue from that due to anxiety or other mental conflict This is rarely difficult for cardiac fatigue is related to effort and is always associated with genuine signs of congestive heart failure

CYANOSIS

Cyanosis is a physical sign rather than a symptom but since it often looms large in a patient s history it may be best considered here

It is well known that a blue colour is imparted to the skin when the capillary blood contains 5 G or more of reduced hæmoglobin per cent (Lundsgaard 1919) Thus with a normal quota of hæmoglobin (15 G per cent) at least one-third of it must be in the reduced form in the capillaries for cyanosis to appear Normal arterial blood is 95 per cent saturated with oxygen i e 14 25 of the 15 G per cent of hæmoglobin in the arterial blood is oxyhæmoglobin and only 0 75 G reduced hæmoglobin The normal mixed venous blood is about 70 per cent saturated with oxygen i e 10 5 G per cent of the hæmoglobin in venous blood is oxyhæmoglobin and 4 5 G reduced hæmoglobin The amount of reduced hæmoglobin in capillary blood is assumed to be the mean between arterial and venous contents thus in a normal individual at rest capillary blood would be assumed to contain $\frac{0\ 75\ G + 4\ 5\ G}{2}$ of reduced hæmoglobin per cent, or 2 6 G per cent The colour of the normal skin and mucous membranes is therefore pink not blue

A corollary of Lundsgaard s thesis is that cyanosis cannot appear in anæmic subjects if the hæmoglobin is less than 33 per cent for even if all the hæmoglobin was then in the reduced form in the capillaries the total amount would still be less than the critical level of 5 G per cent In polycythæmia on the other hand a total of 5 G per cent of reduced hæmoglobin in the capillaries is readily achieved

While the colour of the skin and mucous membranes depends on the amount of reduced hæmoglobin in the capillaries the intensity of the hue is determined by the physical state of the capillaries if they are dilated the colour is rich if they are constricted the colour is pale

Cyanosis may be central or peripheral *Central cyanosis* means that the arterial oxygen saturation is low It can usually be detected clinically when the arterial oxygen saturation falls below 85 per cent With a normal hæmoglobin arterial blood contains 3 G per cent of reduced hæmoglobin when 80 per cent saturated with oxygen If the cardiac output is normal the mixed venous blood is then about 60 per cent saturated and contains 6 G of reduced hæmoglobin per cent The capillary mean thus works out at $\frac{3+6}{2}$ G per cent or 4 5 G per cent

With 85 per cent arterial oxygen saturation a normal cardiac output and 100 per cent hæmoglobin, mean capillary blood contains about $\frac{2\ 25 + 5\ 25}{2}$ or 3 75 G of reduced hæmoglobin per cent Yet in Fallot s tetralogy under just these conditions cyanosis can be detected clinically

In a group of fifteen acyanotic cases of Fallot s tetralogy studied by

the author the arterial oxygen saturation ranged between 87 and 97 per cent at rest anything less than this gave rise to clinical cyanosis except in one case with anæmia

Cyanosis in cor pulmonale due to emphysema may also be clinically detected when the arterial oxygen saturation falls below 85 per cent even when the cardiac output is raised and the arterio venous oxygen difference reduced In six such cases studied by the writer and in which the arterial oxygen saturation ranged between 78 and 87 per cent the mean capillary blood contained an average of 3 9 G of reduced hæmoglobin per cent

These observations do not tally with Lundsgaard s figure of 5 G per cent quoted earlier but the calculations are based on mixed venous samples obtained from the right atrium not from blood obtained directly from the skin veins We have no data on how such samples would effect the calculations It is observed however, that ordinary venous blood containing 4 5 G per cent of reduced hæmoglobin is obviously blue

Central cyanosis occurs in congenital heart disease with right to left shunt as in Fallot s tetralogy in arterio venous fistula of the lung and in certain pulmonary diseases such as severe emphysema which interfere with alveolar function, so that blood passing through the lung is incompletely oxygenated Central cyanosis is usually associated with polycythæmia although this may be masked by a high blood volume as in many case of cor pulmonale If sufficiently severe and long lasting it is also associated with clubbing of the fingers and toes

Peripheral cyanosis may be a manifestation of a low cardiac output the tissues extracting more oxygen from each 100 ml of blood because of the limited supply but heart failure must be extreme before the mean capillary blood contains sufficient reduced hæmoglobin to cause cyanosis in warm territories such as the conjunctivæ Thus of 20 cases with an extreme pulmonary vascular resistance (averaging 15 units or 1 200 dynes sec /cm 5) due to primary pulmonary hypertension (6 cases) or secondary to mitral stenosis (14 cases) chosen at random provided the cardiac output was below 4 litres per minute (in fact it averaged 3 1 /min) the mean capillary blood contained an average of 4 17 G of reduced hæmoglobin per cent None of these cases had cyanosis of the conjunctivæ or other mucous membranes yet the amount of reduced hæmoglobin in the capillaries calculated in the customary fashion was often as high or even higher than that found in cases of Fallot s tetralogy with arterial oxygen saturations around 80 per cent and obvious though mild central cyanosis Mixed venous samples had a higher content and arterial samples a lower content of reduced hæmoglobin in these low output cases than in the examples of Fallot s tetralogy mentioned It follows that cyanosis in warm areas depends much more on the content of reduced hæmoglobin in the arterial blood than in the venous blood It is extremely rare for the arterial oxygen saturation to fall below 85 per cent in these uncomplicated low output states

In view of these findings the term peripheral cyanosis has come to have a narrower meaning than that originally intended it may be defined as cyanosis of cold surfaces due to reduction of peripheral blood flow Thus it is seen chiefly in the skin of the fingers ears nose cheeks and outer side of the lips, it is not seen in the conjunctivæ palate or inner side of the lips or cheeks In heart failure with a low cardiac output considerable vasoconstriction occurs in certain territories in order to maintain the blood pressure the skin being relatively unimportant is one of these territories, and the vasoconstriction is most intense in exposed surfaces which are necessarily cooler The diminished blood flow leads to increased oxygen extraction by the tissues and the subpapillary venous plexuses of the skin must contain a high proportion of reduced hæmoglobin

At the bedside considerable difficulty may be experienced in attempting to distinguish between central and peripheral cyanosis Cyanosis of the conjunctivæ palate tongue and inner side of the lips and cheeks is always central In congenital heart disease cyanosis is certainly central if it is associated with clubbing and polycythæmia and probably central if it deepens on effort In suspected cor pulmonale cyanosis is surely central if associated with warm hands capillary pulsation digital throbbing distended forearm veins and a water hammer type of pulse all manifestations of peripheral vasodilatation Peripheral cyanosis is limited to the ears nose cheeks outer side of the lips hands feet and digits and these parts are cold Clubbing is not associated but polycythæmia may be present if the cardiac output has been low for a sufficient time If doubt still exists despite close attention to these details direct measurement of the arterial oxygen saturation is advised the critical distinguishing level being 85 per cent with normal hæmoglobin

SYNCOPE

There are many causes of transient loss of consciousness and a complete list would include the causes of epilepsy coma concussion and asphyxia but syncope has come to mean transient loss of consciousness of sudden onset due to inadequacy of the cerebral blood flow As so defined syncope may be divided into cardiac vasomotor or vaso vagal cerebral and anoxic forms

Cardiac syncope

Cardiac syncope occurs when the heart through some fault in itself or in its great vessels fails to maintain an adequate cerebral circulation These faults are listed for convenience as follows

1 Cardiac standstill—vagal inhibition
2 Ventricular asystole—Stokes Adams fit
3 Ventricular fibrillation
4 Ball valve thrombus or pedunculated myxoma

5 Aortic stenosis
6 Paroxysmal rhythm changes with extremely rapid ventricular rates
7 Massive pulmonary embolism
8 Cardiac compression from hæmopericardium
9 Low cardiac output states under certain conditions

The practical mechanism whereby the heart fails to fulfil its task varies according to the lesion

In *cardiac standstill ventricular asystole ventricular fibrillation ball valve thrombus* and *pedunculated myxoma* loss of consciousness is abrupt and without warning The attack may occur at any time while the patient is walking standing sitting or lying At first the patient is grey or white flaccid pulseless and motionless The heart sounds are inaudible but respirations may continue In about 10 to 15 seconds anoxic twitchings begin and may develop into convulsions if the attack lasts long enough If recovery does not occur within two minutes death usually results Cardiac and ventricular asystole usually recover well within that time commonly within 5 to 20 seconds but ventricular fibrillation is usually though not necessarily fatal Ball valve thrombus and pedunculated myxoma are rare Return to consciousness is abrupt and complete and is followed by a vivid flush hyper oxygenated blood being flung into a dilated vascular system (reactive hyperæmia)

Similar attacks of uncertain mechanism may occur in *aortic stenosis* As a rule however syncope in aortic stenosis is vasomotor the valve lesion acting merely as a predisposing factor or it is due to a low fixed cardiac output (*vide infra*)

Heart rates up to 200 per minute in *paroxysmal tachycardia* are usually well tolerated but syncope may result if the rate is much faster Speed of over 300 per minute have been recorded The heart has no time to fill or empty properly at these high rates and both cardiac output and blood pressure fall precipitously

Massive pulmonary embolism may cause syncope when more than two-thirds of the circulation is blocked The onset is sudden but rarely so abrupt as in the group just mentioned Moreover it may be preceded by pain or tightness in the chest The duration of unconsciousness is longer being usually measured in minutes or even hours Recovery is at first only partial extreme faintness persisting During the attack the patient is limp grey sweating and breathless The pulse is thready or imperceptible the heart sounds faint or inaudible the blood pressure low or unobtainable

Smaller pulmonary emboli insufficient seriously to embarrass the circulation occasionally cause reflex syncope Such reactions may be prevented by means of atropine Similar attacks may be encountered in cases of acute myocardial infarction These should not be regarded as examples of cardiac syncope for the mechanism is vasomotor

In view of these findings the term peripheral cyanosis has come to have a narrower meaning than that originally intended it may be defined as cyanosis of cold surfaces due to reduction of peripheral blood flow Thus it is seen chiefly in the skin of the fingers ears nose cheeks, and outer side of the lips, it is not seen in the conjunctivæ palate or inner side of the lips or cheeks In heart failure with a low cardiac output considerable vasoconstriction occurs in certain territories in order to maintain the blood pressure the skin being relatively unimportant is one of these territories and the vasoconstriction is most intense in exposed surfaces which are necessarily cooler The diminished blood flow leads to increased oxygen extraction by the tissues and the subpapillary venous plexuses of the skin must contain a high proportion of reduced hæmoglobin

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Stimulation of other receptors that excite a vaso vagal reaction

1 Psychogenic disturbances
2 Carotid sinus compression
3 Extreme pain
4 Cardiac infarction and other sudden visceral catastrophies

This list is by no means complete but it includes most of the common causes of vasomotor syncope

MECHANISM Syncope from hæmorrhage has been thoroughly investigated in blood donors As the blood volume diminishes the venous pressure falls and the cardiac output is reduced Compensatory vasoconstriction may temporarily maintain the blood pressure The faint, which is associated with a sudden fall in blood pressure and pronounced bradycardia appears to be due to sudden vasodilatation in muscle (Barcroft *et al* 1944) This vasodilatation is mediated by vasomotor nerves (Barcroft and Edholm 1944) Whether this reflex is excited by the fall in venous pressure or otherwise is unknown but it is clear that diminution in the blood volume is not directly responsible for the faint for the cardiac output may not alter at the critical moment – the peripheral resistance simply collapses

This sequence of events has also been demonstrated when syncope results from the prolonged application of venous tourniquets to the thighs and probably occurs in all cases of syncope initiated by a critical fall in central venous pressure (Sharpey Schafer 1944) Venous tourniquets on the thighs act as a bloodless venesection by trapping blood in the legs Fainting in soldiers on parade who may have to stand at attention for long periods is believed to depend on similar factors The fall in central venous pressure initiating orthostatic syncope following lumbo dorsal sympathectomy is due to abolition of veno motor tone in the lower half of the body Veno motor paralysis may also be partly responsible for fainting following the injection of ganglionic blocking agents Spontaneous toxic and convalescent ortho static syncope may also be due to loss of veno motor tone

Other forms of postural syncope include fainting in pregnant women when they lie on their backs too long and fainting in certain subjects on adopting the lordotic position The fall in central venous pressure is then attributed to compression of the inferior vena cava by a pregnant uterus or by the liver which is forced against the spine (Bull 1948)

Syncope from chemical agents which cause sudden profound vasodilatation is directly due to collapse of the peripheral resistance The blood pressure falls steeply but the cardiac output may be raised and there may be tachycardia instead of bradycardia Heat gross aortic incompetence and other vasodilatation states predispose to syncope by lowering the peri pheral resistance

Loss of consciousness produced by the intravenous injection of acetyl choline *mecholin* (acetyl beta methylcholine) and *doryl* (carbo amino acetylcholine) is preceded by flushing and a feeling of warmth due to

vasodilatation and by sweating There is commonly abdominal colic nausea or vomiting and desire to micturate or defæcate The blood pressure is low but the pulse rate accelerates Patients may complain bitterly after regaining consciousness saying they feel dreadfully weak', as if they had been ill for months Ordinary therapeutic doses of mecholin and doryl rarely cause syncope the dose must be large and given intravenously Symptoms are relieved at once by 1 to 2 mg of atropine

Syncope from histamine nitrites and diodone is also preceded by flush ing headache and tachycardia Flush syncope may occur spontaneously in women at the menopause or in men at the climacteric Both hot flushes and syncope disappear following treatment with stilbœstrol 0 5 to 1 mg daily

Syncope is not uncommon in hypertensive subjects being treated with hexamethonium or ansolysen It is usually postural and may be severe There is not only collapse of the peripheral resistance but the central venous pressure falls blood being pooled in the periphery The patient should be laid on a couch and tilted head down by means of blocks under the foot end mephentermine 5 mg may be given intravenously and repeated when necessary or noradrenalin may be given by intravenous drip in a strength of 4 or 5 mg per litre the rate being governed by the blood pressure response

The severe collapse that sometimes follows the intravenous injection of too large a dose of quinidine is usually due to its vasodilating action but cardiac standstill or ventricular asystole is occasionally responsible Too large a dose of procaine amide may have a similar effect on the peripheral resistance

The simple psychogenic faint is initiated by emotional disturbance or by stimulation of the afferent component of a conditioned reflex, both result in a powerful autonomic discharge The type of emotion usually responsible is a mixture of fear amazement and curiosity as may arise when a nurse sees a thoracic paracentesis for the first time or when a hypersensitive subject witnesses a street accident The vasomotor centre appears to be suddenly depressed and there are associated cholinergic manifestations the chief result is gross vasodilatation This is certainly not in the skin which is pale and cold but may be in muscle or in the splanchnic bed The peri pheral resistance collapses and the blood pressure sinks rapidly As the cerebral blood flow depends chiefly upon the blood pressure it becomes inadequate and consciousness is lost Spontaneous recovery is inevitable for three reasons first, unconsciousness abolishes the trigger secondly liberated acetylcholine upon which many of the features of the attack may depend is rapidly destroyed by choline esterase thirdly the horizontal position naturally adopted by an unconscious subject increases the cardiac output and is favourable to the cerebral blood flow

Carotid sinus syncope is said to be of four main types which may be repro duced by carotid sinus compression (Weiss and Baker 1933 Ferris Capps

and Weiss 1935) First syncope may be due to cardiac standstill Second loss of consciousness may be associated with a gross fall of blood pressure and with marked slowing of the pulse rate If the latter is restored to normal by atropine consciousness is not regained if the blood pressure is restored by any means consciousness returns even though the pulse remains slow It is the low blood pressure and not the slow pulse rate which is responsible for the syncope This type corresponds to vaso vagal syncope Third carotid sinus pressure may induce syncope associated with a profound fall in blood pressure without slowing of the pulse rate It is doubtful if there is any fundamental difference between these two forms of attack, for not infrequently the first type merges into the second indeed it has been suggested that initial slowing of the heart occurs in all cases but that subsequent quickening resulting reflexly from the low blood pressure may occur so rapidly as to mislead the observer

Weiss and Baker describe a fourth type of syncope resulting from carotid sinus pressure in which the blood pressure and pulse rate are unchanged and refer to it as cerebral syncope This appears to be allied to epilepsy for no reduction of cerebral blood flow can be demonstrated

Spontaneous carotid sinus syncope may occur in rare instances The organ is hypersensitive and may be excited by sudden pressure of the neck against a tight collar The condition may be cured by carotid sinus denervation

Reflex syncope from pain myocardial infarction pulmonary embolism etc is similar in mechanism to the simple psychogenic faint

CLINICAL FEATURES Spontaneous vasomotor syncope is ushered in with numerous signs and symptoms of autonomic disturbance e g yawning pallor, sweating coldness of the skin a sinking feeling in the pit of the stomach general muscular weakness subjective changes of temperature a feeling as if the blood was all rushing downwards epigastric discomfort and nausea desire to micturate or defæcate a feeling of light headedness and so forth

Patients are aware of imminent loss of consciousness and although the onset of the faint may be described as quick or sudden it is never abrupt

Susceptible individuals faint when standing up rarely when sitting and practically never when lying they faint in company or when in reach of company, rarely when alone They are especially liable to attacks in closed spaces in church in the cinema and in circumstances that provoke emotional disturbance

The muscles are flaccid in vasomotor syncope so that the patient collapses like a house of cards his final position being determined by gravity he lies limp and inert in a sprawled or crumpled position and may well be on his back He is deathly white and often cold and clammy The eyes may be open or closed the position of the upper lid being governed by gravity The pupils are dilated and may be insensitive to light the reflexes and tendon jerks absent or depressed The tongue is never bitten but

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urine may be voided The essential feature is the low blood pressure which may be in the region of 50 or 60 mm Hg more often it cannot be determined The pulse rate is slow normal or quick In severe attacks slight twitching may be seen but is uncommon

The duration of vasomotor syncope is variable and though usually measured in minutes it may last much longer even up to an hour Consciousness is regained gradually and the patient then feels weak and ill he may complain of headache nausea or vomiting of a continued feeling of faintness or light headedness of trembling and shaking or of cold sweats He rarely recovers completely for half an hour or so and usually likes to lie down until he is better

Historically the chief difficulty is to distinguish vasomotor syncope from cardiac or cerebral syncope and from epilepsy

Meniere s syndrome or aural vertigo is usually recognised by its spinning quality but occasionally there is no spinning but merely unsteadiness imbalance or sudden attacks in which the subject is thrown violently forwards or backwards Consciousness is rarely lost however and either tinnitus or deafness is usually associated

Cerebral syncope

Cerebral syncope may result from cerebral vascular spasm or transient occlusion The fault is local

Hyperventilation syncope is the best example Forced breathing results in carbon dioxide washout with secondary alkalæmia Carbon dioxide ordinarily helps to maintain an adequate degree of cerebral vasodilatation (Norcross 1938) its lack causes cerebral vasoconstriction This induces dizziness within a minute in most normal individuals undergoing forced breathing If hyperventilation is maintained long enough syncope may occur Spontaneous attacks are seen in hysteria and sometimes in encephalitis lethargica There is usually associated vasoconstriction in the extremities with pallor cyanosis and tingling of the fingers and toes and there may be tetany The blood pressure is maintained or raised owing to vasoconstriction the latter tending to prevent reduction of cerebral blood flow

Forced breathing may be used as a test in cases of syncope to discover whether an attack can be reproduced It should be remembered however that epilepsy is sometimes excited by hyperventilation so that the diagnosis depends upon the nature of the induced attack not upon the simple fact that consciousness is lost The effects of spontaneous hyperventilation may be quickly abolished by the inhalation of carbon dioxide This may be accomplished by breathing in and out of a paper bag or long rubber tube

Loss of consciousness due to hypertensive encephalopathy or to cerebral vascular lesions with or without associated spasm of cerebral vessels is usually called coma unless convulsive epilepsy occurs Embolism however especially when due to air or fat may provoke an attack which fulfills the

definition of syncope The onset is abrupt and recovery may be remarkably quick and complete if the embolism moves on or if spasm passes off suddenly

Loss of consciousness occasionally occurs in Menière s syndrome but is then probably a vaso vagal reaction

Bilateral carotid compression an old ju jitsu trick is a most effective way of inducing unconsciousness in an adversary

Anoxic syncope

Loss of consciousness resulting from most causes of anoxia is described as asphyxia or coma Anoxic syncope however may occur in congenital heart disease with right to left shunt, especially in Fallot s tetralogy and is attributed to diminished peripheral resistance increased pulmonary resistance or a fall in total cardiac output A vaso vagal turn may have a disastrous effect in Fallot s tetralogy for the drop in blood pressure at once increases the amount of blood shunted from right to left and the sudden fall in arterial oxygen saturation may further depress the vasomotor centre so that a vicious circle is established patients may die in this way In four cases of anoxic syncope investigated by the writer however an increase of pulmonary resistance seemed to be responsible for the attacks Loss of consciousness was associated with extreme cyanosis disappearance of the characteristic pulmonary systolic thrill and murmur and no fall in blood pressure In one instance the arterial blood was almost completely unsaturated Raising the blood pressure well above normal by means of methedrine had no effect on the arterial oxygen saturation and did not restore consciousness These cases behaved as if there were transient functional pulmonary atresia whether the obstruction was due to temporary closure of the infundibulum itself or to pulmonary vasoconstriction could not be determined No structural block by a clot for example was found at necropsy in the case that died in the attack The writer has also witnessed syncope in Fallot s tetralogy resulting from an ill advised venesection since the blood pressure fell sharply however the increased cyanosis that accompanied loss of consciousness could well have been due to a vaso vagal mechanism and not to reduction of total cardiac output *per se*

Tussive syncope (from a prolonged attack of coughing) may be anoxic or asphyxial in one sense but is more properly ascribed to failure of cardiac filling due to an extremely high intrathoracic pressure which totally obstructs the venous return at the thoracic inlet

PALPITATIONS

Palpitations may be rapid and regular with abrupt onset and offset as in paroxysmal tachycardia rapid and chaotic as in auricular fibrillation or fleeting and repetitive as with ectopic beats in such cases the abnormal rhythm can usually be recognised from the description of the sensation Palpitations may be heavy rather than fast or irregular however and then

an increased stroke volume may be responsible Physiological or pathological hyperkinetic circulatory states aortic or mitral incompetence patent ductus ventricular septal defect and atrial septal defect may cause heavy thudding of this kind In both types the sensation seems to be caused by a radical change in the natural stroke action of the heart it is the unusual movement of the heart within the thorax that is felt not an increased force of cardiac contraction nor more forcible valve closure Thus palpitations are not a feature of aortic stenosis or pulmonary stenosis nor of malignant hypertension or primary pulmonary hypertension The point may be further elaborated in respect of palpitations due to ectopic beats It is usually said that it is not the ectopic beat which is felt but the strong beat following the compensatory pause Anyone who has himself experienced ectopic palpitations is invited to question this He may well beg to disagree the quick beat out of time with the heart improperly filled gives rise to the first sensation and this alone may be felt or it may be followed by a second sensation due to the beat of the over filled heart after the pause A run of ectopics makes it only too obvious that the quick beat is felt

A third type of throbbing is vascular This may be arterial as in aortic incompetence or venous as in gross tricuspid incompetence It is again the unusual movement within the tissues that is felt Tactile perceptors in the skin may be stimulated by pressure from within as can be demonstrated easily enough during the passage of a venous catheter for this procedure causes no sensation at all unless the catheter tip comes into indirect contact with the skin in the arm neck or thorax

Patients may also complain of a beat in the head which is really a sound It may be single an internal phase III Korotkow sound associated with vasodilatation or it may be double when both first and second heart sounds are heard The symptom usually occurs in bed at night

Palpitations of any kind naturally draw the patient s attention to his heart and he may soon begin to question its integrity this leads to anxiety and since emotional turmoil is the commonest cause of the symptom at once closes a vicious circle

HÆMOPTYSIS

Although hæmoptysis may occur in a wide variety of cardiovascular diseases it only does so under strictly defined circumstances

(1) A necrotic arterial lesion may rupture, as in disseminated lupus Pulmonary tuberculosis may accidentally complicate any form of heart disease this accounted for hæmoptysis in two out of three cases of A S D in the writer s series in which this symptom occurred (2 per cent) An arterio venous aneurysm may rupture or a syphilitic or mycotic aneurysm may rupture into the bronchus Pulmonary lesions like bronchiectasis or bronchial carcinoma should not be overlooked when hæmoptysis occurs unexpectedly in association with heart disease All these hæmorrhages are essentially necrotic

(2) Hæmoptysis may occur suddenly as the first symptom of mitral stenosis and may be precipitated by effort or pregnancy This kind of pulmonary apoplexy has been attributed to rupture of small pulmonary or broncho pulmonary anastomotic venules as a result of a sudden rise of left atrial pressure Such hæmorrhages tend to cease as the pulmonary veins thicken in response to the rise of pressure within them, or when the pulmonary vascular resistance exceeds 10 units (800 dynes sec /cm 5) and so protects the pulmonary venous system from developing too high a pressure (Wood 1954)

(3) Bloodstained sputum may accompany an attack of paroxysmal cardiac dyspnœa in mitral stenosis or left ventricular failure and may be attributed to intense pulmonary venous congestion (congestive hæmoptysis) In these cases the dyspnœa is much more important than the hæmoptysis Blood-spitting in an attack of bronchitis complicating mitral stenosis has a similar significance and the pink frothy sputum of acute pulmonary œdema is closely related

(4) Frank hæmoptysis may be caused by pulmonary infarction This is usually a late manifestation of heart disease for the phlebothrombosis in the legs from which the responsible embolus springs is apt to be a complication of congestive heart failure proper Emboli from right sided bacterial endocarditis may also cause hæmoptysis from small areas of infarction

Hæmoptysis rarely if ever results from uncomplicated pulmonary plethora in patent ductus V S D and A S D nor is it a symptom of pulmonary hypertension primary secondary or hyperkinetic It may occur with passive pulmonary hypertension but here it is the high pulmonary venous pressure that matters not the arterial

Hæmoptysis in essential hypertension is sometimes due to posterior epistaxis in other cases however this can be excluded and the site of the hæmorrhage is then a matter for conjecture It is not common

RECURRENT BRONCHITIS

Trivial upper respiratory tract infections may rapidly develop into florid bronchitis in two main types of disturbed physiology in cardiovascular disease pulmonary plethora and pulmonary venous congestion

Pulmonary plethora i e an increased pulmonary blood flow occurs typically in patent ductus and ventricular or atrial septal defect pulmonary venous congestion in left ventricular failure and mitral valve disease It is suggested that the violent reaction to trivial infection is due to the hyperæmic state of the pulmonary circulation Most diseases require both an etiological agent and some tissue reaction a pathogenic agent may be harmless Thus spirochætal aortitis does not occur in syphilis although the aorta may contain numerous spirochætes

there is no tissue reaction again amœbæ do not necessarily cause dysentery when they take up their abode in the human colon but only when reactive ulcerative colitis develops Hyperæmia is one of the fundamental reactions to infective agents and a major part of what is known as inflammation if the lung is already hyperæmic an inflammatory reaction would be expected to be intense

Recurrent bronchitis is not a feature of pulmonary ischæmia in congenital anomalies with right to left shunt or in low output states for example it is uncommon in Fallot s tetralogy and primary pulmonary hypertension

Recurrent bronchitis is of course an important feature of anoxic cor pulmonale but here it has a causal role

Both chronic cough and bronchitis may also result from compression of the right or left main bronchus from aneurysm of the aorta or pulmonary artery or from aneurysmal dilatation of the left atrium

INSOMNIA

Many patients with heart *failure complain bitterly* of insomnia Since the physiology of sleep is still improperly understood little would be gained by discussing the mechanism of the insomnia But there are two obvious symptoms which may interrupt sleep in cases of heart failure—paroxysmal cardiac dyspnœa and Cheyne Stokes breathing

Nocturnal dyspnœa in left ventricular failure and mitral valve disease may be abolished by means of a low sodium diet and mercurial diuretics and it has been well said that the best cure for insomnia in these cases is mersalyl (Evans)

Cheyne Stokes breathing tends to wake the patient during the dyspnœic phase of each respiratory cycle The symptom can be very troublesome because it is aggravated by morphine barbiturates and indeed by sleep itself Fortunately however it can usually be abolished by aminophylline preferably given as a suppository in a dose of 0 4 G at night Aminophylline has the double advantage of preventing paroxysmal cardiac dyspnœa as well

Thus although barbiturates may have *to be used for the insomnia of* heart failure better results are usually achieved by the efficient treatment of the heart failure itself

SYSTEMIC EMBOLISM

Under certain circumstances a clot may form in the left side of the heart or in a pulmonary vein and if liberated must find its way into some cerebral visceral or peripheral artery The chief causes of thrombosis in the cavity of the left ventricle are cardiac infarction and isolated myocarditis in the left atrium mitral valve disease and auricular fibrillation and in the aortic or mitral valve bacterial endocarditis The commonest cause of embolism is undoubtedly *mitral valve disease with auricular fibrillation*

There is increasing evidence that only a fresh clot is liable to be set free and that in mitral valve disease this fresh clot is most likely to form within the first few days of the onset of uncontrolled auricular fibrillation whether paroxysmal or permanent The embolism may occur while the auricle is still fibrillating or soon after normal rhythm is resumed spontaneously or in response to quinidine therapy

Cerebral embolism

The clinical features of cerebral embolism differ from those of cerebral thrombosis in three ways first the attack is abrupt rather than sudden in onset often with loss of consciousness second the symptoms are maximal at the start and third remarkable recovery may take place within a few minutes or hours In addition one of the known underlying causes of systemic embolism should be apparent

Treatment consists of doing everything possible to promote an effective cerebral circulation and to prevent secondary thrombosis The patient should be nursed flat if the state of the heart allows it Uncontrolled auricular fibrillation and congestive heart failure should be treated quickly and efficiently to encourage the maximum cardiac output Oxygen with 5 per cent carbon dioxide may be inhaled with advantage and the blood pressure must be maintained if necessary by means of a noradrenaline intravenous infusion at a rate of approximately 10 μg per minute mephentermine (wyamine) 35 mg intramuscularly or some other pressor amine for the cerebral blood flow depends chiefly upon the arterial carbon dioxide content and the blood pressure Vasodilators (to relieve vascular spasm) are not recommended for they are more likely to act peripherally than on the cerebral vessels and by lowering the blood pressure may have an adverse effect on cerebral flow Anticoagulants have often been withheld on the grounds that they might induce hæmorrhage in an area of cerebral softening but there is little factual evidence to support this view and in the writer s opinion they should be given both to prevent secondary thrombosis and further embolism

Visceral embolism

An embolus may lodge in a mesenteric splenic renal coronary or other visceral artery

Mesenteric embolism is characterised by sudden severe epigastric pain with or without shock The patient presents with an acute abdomen but on examination there is no guarding and but little tenderness Within a few hours malena appears the blood being dark red in colour Symptoms and signs of sub acute or complete intestinal paralysis follow with vomiting and increasing distension The outlook is bad in the more severe cases death occurring in a few days In less severe cases however despite evidence of ileus and even though malena may be extensive recovery may occur within the week

there is no tissue reaction, again, amoebae do not necessarily cause dysentery when they take up their abode in the human colon, but only when reactive ulcerative colitis develops. Hyperaemia is one of the fundamental reactions to infective agents and a major part of what is known as inflammation. If the lung is already hyperaemic an inflammatory reaction would be expected to be intense.

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SYSTEMIC EMBOLISM

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usually established by the deep femoral artery When collateral vessels are atherosclerotic or otherwise diseased however as is common in the aged, these principles do not apply for then a relatively small embolism may precipitate gangrene Each case must be considered carefully on its merits Pain is due to ischæmia of working muscle in the affected territory Thus an embolus may lodge quietly in a resting limb and cause no pain until the limb is actively moved If there is sufficient ischæmia of nervous tissue pain at rest paræsthesia or peripheral anæsthesia may be present On examination the affected limb is colder than its fellow and may be pale or cyanosed The distal vessels are impalpable Methodical palpation of the vessels in a proximal direction may reveal the site of the embolism for above it pulsation is normal

The problem in every case is whether to advise embolectomy or con servative treatment Good judgment would take into account the site of the embolus the age of the patient the presence or absence of peripheral vascular disease such as atherosclerosis the objective findings concerning the immediate state of the peripheral circulation and the fact that if an operation is to be performed it should not be delayed more than six hours There are three other points of peculiar importance which should also be considered First an embolus often moves on from a position of danger to one of safety It is not wise to attempt to milk it down the limb because the embolus may then break up and its fragments may block several distal vessels and so interfere seriously with collateral circulatory efficiency Second there may be considerable vascular spasm associated with an embolus so that initial ischæmia may be disproportionate to the size of the vessel blocked Third in cases associated with heart failure and auricular fibrillation with rapid ventricular rate an inadequate collateral circulation may be made sufficient by improving the cardiac output Dramatic effects may be obtained in such cases by intravenous digoxin or strophanthin when a critical situation may be turned within half an hour

The fact is that most of these cases do better than is generally supposed The wisest course is to start intensive medical treatment immediately the diagnosis is made Morphine or pethidine heating the body with an electric cradle or hot water bottles and various vasodilators such as eupaverine or priscol are helpful Hypertonic saline is rarely practical in cardiac cases If after two hours of such treatment the peripheral circulation as judged by the colour temperature and function of the limb remains in jeopardy the surgeon should be invited to perform embolectomy Once this decision has been made the physician should increase rather than decrease his efforts to make the operation unnecessary and in close co operation with the surgeon should be prepared to ask for a little more time if there is any sign of improvement A good surgeon however will be anxious to avoid delay if in his own opinion conservative measures are proving ineffective

Reluctance to advise embolectomy is based on three precepts first if an operation is to be performed heparin may have to be withheld

anticoagulants are highly desirable to prevent post embolic thrombosis and further embolism second it is embarrassing to witness exposure of a vessel which is found to be pulsating freely by the time it is reached third, arteriotomy is not devoid of the risk of post operative thrombosis Nevertheless embolectomy is essential if the limb is really in danger

OTHER SYMPTOMS

Pulmonary embolism usually secondary to phlebothrombosis in the legs is a common complication of heart failure with a low cardiac output and is discussed fully in Chapter XVII

Cardiac cachexia sometimes obscured by œdema and swelling of the abdomen is a common late manifestation of chronic heart failure It occurs especially in lingering cases of aortic, mitral or tricuspid stenosis

Cerebral symptoms include varying grades of dementia in advanced hypertension attacks of encephalopathy in malignant hypertension and confusional or frankly psychotic states attributed to anoxia diminished cerebral blood flow or impaired hepatic function as for example in cor pulmonale following operations on the heart in which the blood pressure has dropped to low levels for too long a period and in severe low-output heart failure respectively

Swelling of the abdomen due to gross enlargement of the liver with or without ascites may complicate chronic heart failure from any cause but is seen especially in constrictive pericarditis severe tricuspid stenosis and advanced cases of functional tricuspid incompetence associated with chronic right ventricular failure Cirrhosis of the liver in alcoholics with heart failure may provide independent grounds for ascites and thrombosis of the hepatic vein may complicate heart failure

Jaundice and vomiting complicating heart failure are discussed in Chapter VII

Oligemia and nocturia are also discussed under Heart Failure and nocturia again in the chapter on Hypertension

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CHAPTER II

PHYSICAL SIGNS

THERE are two methods of examining a patient the first begins at the top of the head and ends with the toes a method often adopted for the sake of convenience the second is to examine the various systems of the body one by one in logical sequence The procedure recommended here is concerned only with the cardiovascular system but it is essential of course that all other systems be examined

GENERAL INSPECTION

While extracting the history the physician should be making a preliminary general inspection He should pay particular attention to the head and neck looking for goitre and for the eye signs of thyrotoxicosis for Corrigan s sign and especially for jugular pulsation He will note the general build and appearance of the patient his attitude and demeanour and should form some idea of his character He should observe plethora, pallor or cyanosis He may see that respiration is hurried irregular shallow or wheezy or he may detect the tell tale sigh of emotional tension He is sure to glance at the hands noting their posture shape colour and behaviour he may discern clubbing of the fingers spooning of the nails tremor or palmar sweating All these things and many others he will learn to observe without effort taking note of them without seeming to do so, and in such a limited survey may be put on the track of the correct diagnosis and be forewarned where to look most diligently for further signs

THE ARTERIAL PULSE

It is customary to examine the pulse first at the wrist and to consider it in terms of speed rhythm tension amplitude and quality at the same time it is convenient to note the state of the arterial wall Whilst speed and rhythm may be checked by auscultation of the heart and tension by sphygmomanometry the quality and amplitude of the pulse wave can only be analysed in peripheral vessels and are features of great diagnostic importance

The most convenient and revealing pulse to examine is the right brachial it is best felt with the thumb of the right hand, the physician being on the patient s right side The quality of the brachial pulse can only be learned by experience What is felt is a pressure wave, and to appreciate it fully it is necessary to vary the pressure which the thumb exerts upon the artery until maximum movement is detected This implies exerting a force equal

to the diastolic arterial pressure The upstroke of the pulse or percussion wave is smooth and fairly sharp without being abrupt and occupies about 0 08 sec (range 0 06 to 1 0 sec) the peak of the wave is momentarily sustained, so that arterial pressure curves have a rounded summit occupying 0 06 to 0 12 sec and the downstroke is initially fairly quick but not precipitous, the whole movement being smooth and uniform (fig 2 01)

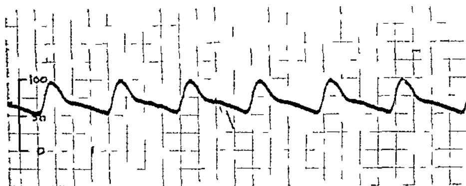


Fig 2 01—Normal arterial pulse in a child

Pulsus parvus

A pulse wave of small amplitude means that systolic and diastolic pressures are nearer one another than usual i e they are approaching the mean arterial pressure This is a sign of vasoconstriction and generally implies a low cardiac output In normal subjects it may be due to cold or anxiety It occurs locally in the arteries of the legs in coarctation of the

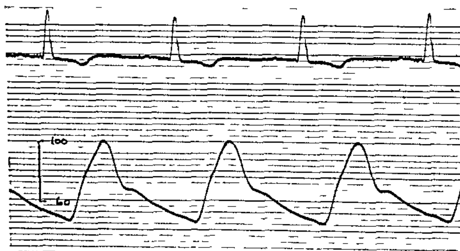


Fig 2 02—The anacrotic pulse of aortic stenosis the percussion wave is dwarfed occupies 0 1 second the large blunt peak builds up slowly the maximum pressure being reached until 0 24 second after the onset (major time intervals 0 1 sec)

aorta and in any artery distal to partial occlusion. In disease it is characteristic of severe hypertension aortic stenosis cardiac infarction mitral stenosis extreme pulmonary hypertension severe pulmonary stenosis, tricuspid stenosis Pick s disease pericardial effusion myocarditis and any form of low output failure

Bounding pulse

A large pulse wave of good form means a high pulse pressure associated with an increased blood flow and is seen characteristically in the hyperkinetic circulatory states

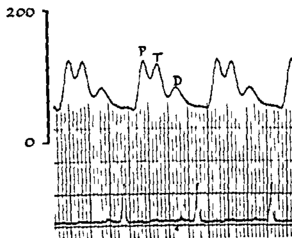


Fig 2 03—Pulsus bisferiens external arteriogram showing two peaks in systole P being the percussion wave and T the tidal wave they are followed by the dicrotic wave

Anacrotic pulse

A slow upstroke associated with a pulse wave of low amplitude is typical of aortic stenosis (fig 2 02) Sometimes a notch can be felt on the upstroke this is the *anacrotic* pulse (or in full anadicrotic—ανα up δις twice κροτος beat)

Pulsus bisferiens

In combined aortic stenosis and incompetence a double beat during systole may be very pronounced (fig 2 03) it shows up well in the ordinary external arteriogram when some pressure is applied to the surface of the artery by means of the pick up device but the trough between the two peaks usually disappears in intra arterial pressure tracings being replaced by a short plateau or shoulder (fig 2 04) The second component of the beat has been attributed to a tidal wave the onset of the percussion wave being reflected back from the periphery before the tail of the percussion wave has passed the meeting of the two having a summation effect (Bramwell 1947)

Dicrotic pulse

In the better known form of twice beating pulse the percussion wave is followed by a palpable secondary wave after aortic valve closure (fig 2 05) In normal individuals the downstroke of the pulse wave is interrupted by a notch (dicrotic notch) representing aortic valve closure but the small positive pressure wave (dicrotic wave) that follows the notch or distorts

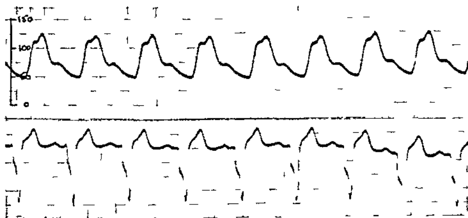


Fig 2 04—Intra arterial pressure tracing of the pulsus bisferiens The dip between percussion and tidal waves is replaced by a plateau

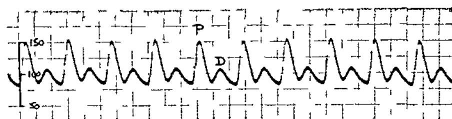


Fig. 2 05—Intra arterial pressure tracing of a typical dicrotic pulse (D)

the contour of the descent cannot be felt clinically The dicrotic pulse is encountered chiefly in patients sick with some fever such as typhoid the peripheral resistance is low the blood pressure low, the arteries lax and the cardiac output probably normal

Water hammer pulse

This aptly describes the combination of an abrupt percussion wave *ill sustained crest, and rapid collapse (fig 2 06) A water hammer is a* hermetically sealed tube containing a vacuum partly filled with water when the tube is inverted quickly the water drops abruptly and imparts a palpable shock to that end of the container A pulse having this charac teristic quality indicates a low filling resistance in the reservoir into which the left ventricle pumps its contents In health a low resistance is always peripheral and means vasodilatation usually due to heat exercise emotional disturbance pregnancy or alcohol Peripheral vasodilatation is characteristic of the hyperkinetic circulatory states such as thyrotoxicosis anæmia beri beri, hepatic failure and anoxic cor pulmonale Peripheral resistance is lowered by a leak in the arterial side of the circulation e

in arterio venous fistula patent ductus aortic incompetence mitral incompetence and possibly ventricular septal defect The physiological counterpart of an arterio venous fistula may also occur in the thyroid gland in thyrotoxicosis (spontaneously or as a result of anti thyroid drugs) in the uterus during pregnancy and in bone in Paget s disease Again peripheral

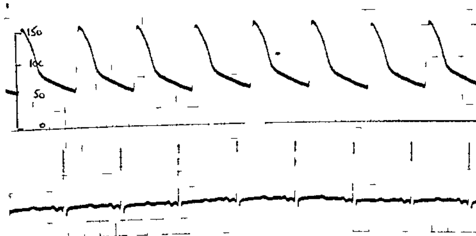


Fig 2 06—Intra arterial pressure tracing of a water hammer pulse in a case of patent ductus arteriosus Note the singularly abrupt wave front

vasodilatation tends to accompany most of the conditions mentioned with the teleological effect of encouraging forward flow in competition with the leak Finally a water hammer pulse often accompanies complete heart block, in which an unusually large volume of blood is flung into a relatively empty arterial reservoir each beat

The amplitude of the water hammer pulse varies considerably in these different conditions being highest in aortic incompetence, heart block and the hyperkinetic circulatory states (physiological or pathological) and lowest in mitral incompetence The collapse occurs in the latter part of systole and the dicrotic notch is usually displaced towards the base line In the majority the systolic blood pressure is somewhat raised and the diastolic low

Pulsus alternans

Alternate larger and smaller beats with normal rhythm are characteristic of severe systemic hypertension or left ventricular failure The mechanism is discussed in Chapter VII Similar alternation may occur in the pulmonary arterial pulse right ventricle and right atrium in severe pulmonary hypertension or stenosis (fig 2 07) There is no change in alternate electrocardiographic complexes and as a rule the phenomenon cannot be recognised by means of auscultation A bout of alternation is frequently precipitated by an ectopic beat in susceptible cases

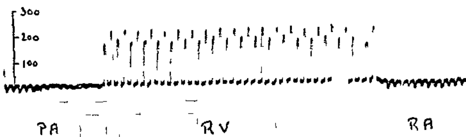


Fig 2 07—Right ventricular alteration in a case of severe pulmonary stenosis (Paper speed = 5 mm per sec)

Pulsus paradoxus

The pulse normally quickens during inspiration and slows during expiration but it does not alter appreciably in volume in chronic constrictive pericarditis and in tense pericardial effusion however it may become very small or disappear altogether during inspiration The mechanism is discussed in Chapter XIII

Pulsus bigeminus

Alternate ventricular ectopic beats results in coupling each pair of beats consisting of a normal or large pulse followed by a small one

The pulse in other arteries

The pulse should be checked in all the palpable major arteries on both sides i e in the radials brachials carotids femorals popliteals posterior tibials and dorsal arteries of the feet

Difficulty in locating the radial artery may be due to its taking an aberrant dorso lateral course *Weakness on one or other side* usually denotes proximal compression as from aneurysm of the aorta but a weak left radial pulse may be due to an ectopic origin and aberrant course of the left subclavian artery

The carotids may present an unusual degree of pulsation associated with coarctation of the aorta Corrigan s sign of aortic incompetence kinking from atherosclerosis or a thrill or shudder indicating aortic stenosis

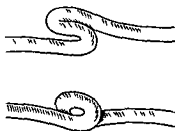


Fig 2 08—Two types of kinked carotid

CORRIGAN S SIGN consists of abrupt distension and quick collapse of the carotids the movement being of high amplitude It is discovered by inspection (Corrigan 1832) not by palpation and should not strictly be confused with a palpable water hammer pulse

CAROTID KINKING superficially resembles a rounded pulsating aneurysm

at the base of the right common carotid A short segment of the vessel is looped back sharply on itself to give this impression (fig 2 08) It is caused by elevation of the aortic arch as a result of hypertension or atherosclerosis so that the carotids, particularly the right come to be too long for the distance they occupy The lesion is seen especially in obese women in whom the heart is also elevated

Routine palpation of the arteries in the legs would insure the immediate recognition of coarctation of the aorta in nearly all cases *diminished and delayed femoral pulsation* being characteristic and almost pathognomonic The presence of pulsation in the vessels of the feet should always be recorded if only for subsequent reference

THE EXTREMITIES

Further information of the kind partly given by the arterial pulse may be obtained from examining the extremities particularly the fingers hands and forearms

Signs of vasodilatation

DIGITAL THROBBING indicates vasodilatation and may be detected by picking up all the fingers of the patient s right hand with all the fingers of the examiner s right hand so that the two sets grip each other gently finger to finger in a flexed position

CAPILLARY PULSATION has a similar significance and is best demon strated by transilluminating the tip of the middle finger or thumb by pressing a pocket torch into the pad underneath and shading the nail bed from daylight with the flexed fingers of the examiner s other hand

WARM HANDS are associated with these signs of vasodilatation and if the blood flow is increased *the forearm veins are usually distended*

Vasodilatation occurs in all the physiological and pathological hyper kinetic circulatory states and in all conditions which may give rise to the water hammer pulse

Signs of vasoconstriction

COLD HANDS are associated with peripheral vasoconstriction and when the blood flow is diminished the *forearm veins become spidery* Peripheral vasoconstriction may be due to cold when it helps to prevent loss of heat from exposed surfaces to apprehension as part of a general response or to a low cardiac output when it helps to maintain the blood pressure

Other circulatory signs

THE COLOUR OF THE HANDS gives less information concerning blood flow and arterial tone As a general rule the colour is pink when there is vaso dilatation and pale or blue when there is vasoconstriction But the palms of the hands may be bright red in certain cases of low output heart failure en hepatic function is sufficiently disturbed and the hands are pale in

anæmia and blue in anoxic cor pulmonale although the cardiac output may be high and the arterioles dilated Richly coloured often cyanosed hands are seen in polycythæmia vera

DIFFERENTIAL CYANOSIS between the hands and feet the hands being pink and the feet blue is pathognomonic of pulmonary hypertension with right to left shunt via a patent ductus arteriosus

THE RAYNAUD PHENOMENON (Raynaud 1862) defined by Hunt (1936) as intermittent pallor or cyanosis of the extremities precipitated by exposure to cold without blockage of the large peripheral vessels and with nutritional lesions if present at all limited to the skin cannot be described here in detail It must be stated however that at least one third of patients with myxœdema suffer from this disorder and that it is not infrequently the first symptom of the disease Hypersensitivity to cold and a reduced peripheral blood flow are presumably responsible Raynaud s phenomenon is not uncommon in other low output states such as hypertensive heart failure and advanced mitral stenosis on the other hand it is rare in thyro*toxicosis and other hyperkinetic circulatory states*

THE SCLERODERMA OF THE FINGERS (acrosclerosis) that may be associated with Raynaud s disease is usually regarded as a vasomotor trophic change but may be associated with more widespread lesions particularly in the skin of the face and neck and in the submucosal connective tissue of the mouth and œsophagus (Olsen O Leary and Kirklin 1945) Scleroderma however may also involve the heart (Weiss *et al* 1943) In the majority of such cases the extremities have shown pigmentation a rheumatoid type of arthritis and Raynaud s syndrome in addition to the smooth glossy drum tight skin of scleroderma (fig 2 09)



Fig 2 09—Sclerodactyly

Changes in the nails

CLUBBING OF THE FINGERS AND TOES may occur in cyanotic forms of congenital heart disease bacterial endocarditis and anoxic cor pulmonale also of course in suppurative lesions of the lungs such as pulmonary abscess and bronchiectasis and bronchial carcinoma clubbing may also be hereditary, and has been reported in association with sprue cirrhosis of the liver, post operative myxœdema and syphilitic aneurysm (where it may be unilateral) Advanced clubbing is obvious the tips of the digits beyond the root of the nail being swollen rounded and congested there being an overgrowth of the soft tissues of the nail bed and hyperæmia The best sign of mild clubbing is probably obliteration of the normal angle between the base of the nail and the skin proximal to it (fig 2 10) Clubbing is rare in infancy even when cyanosis is intense but is common enough in Fallot s tetralogy by the age of two or three It may develop very quickly under appropriate circumstances in two to three weeks for example in cases of pulmonary abscess and may disappear equally quickly when its cause is radically removed e g when the arterial oxygen saturation is restored to normal by means of pulmonary valvotomy or infundibular resection in cases of Fallot s tetralogy The precise cause of clubbing is still unknown but it appears to be related to an increase of blood flow in the terminal digits (Mendlowitz 1938)



Fig 2 10—Clubbed fingers showing disappearance of the normal angle between the skin and nail

KOILONYCHIA (spooning of the nails) is a well known sign of iron deficiency anæmia the nails are flattened even concave fragile and tend to split longitudinally (fig 2 11) They are rapidly restored to normal as the anæmia improves with iron therapy Koilonychia has also been reported

in thyrotoxicosis without anaemia (Cooke and Luty 1944) and is sometimes encountered in apparently normal individuals

OPAQUE WHITE NAILS have been reported in hepatic cirrhosis (Terry 1954) including cardiac cirrhosis



Fig 2 11—Koilonychia The spoon shaped nails are holding a drop of water



Fig 2 12—Arachnodactyly

Congenital deformities

ARACHNODACTYLY or spider fingers (fig 2 12) first described by Marfan (1896) is an hereditary and familial disorder of mesoblastic growth and in its complete form is characterised by elongated spidery fingers and toes thin facies tall lean build muscular hypotonia (and its consequences, e g scoliosis and flat feet) dislocation of the lenses high arched palate, deformed teeth and pigeon chest (Rados 1942) Cardiac anomalies, especially hypoplasia of the aorta (with or without dilatation aneurysm dissection or rupture) and atrial septal defect are associated in 40 to 45 per cent of cases and patients have an increased liability to rheumatism and rheumatic mitral or aortic valve disease (Reynolds 1950 Goyette and Palmer 1953)

SYNDACTYLY and POLYDACTYLY may also be hereditary or familial and may be associated with congenital heart disease

Arthritis of the hands and feet

RHEUMATIC FEVER in adults not infrequently attacks the small joints of the hands and may be mistaken for rheumatoid

RHEUMATOID itself may cause pericarditis with or without effusion

Historical or objective evidence of previous *gout* should be noted partly because in susceptible individuals an attack may be readily provoked by dehydration resulting from mercurial diuretics or a strict low sodium regime unless special precautions are taken

PULMONARY OSTEOARTHROPATHY associated with central cyanosis and an increased blood flow to the extremities is an uncommon complication of advanced anoxic cor pulmonale (see Chapter XVIII) The wrists elbows ankles and knees may all be involved as well as the small joints of the hands and feet

Heberden s nodes or other evidence of osteoarthritis are of no cardio vascular significance

Nodes

OSLER S NODES are small tender erythematous transient and often palpable skin lesions characteristic of bacterial endocarditis They occur especially in the pads of the fingers or toes the palms of the hands or soles of the feet and are due to infected emboli (Osler 1909)

RED TENDER MACULES biopsies of which may also yield positive cultures are equally if not more common in bacterial endocarditis

LARGER INFLAMMATORY NODES resembling a septic finger in the pre suppurative stage constitute a third type of peripheral lesion in this disease

DISSEMINATED LUPUS may give rise to painful erythematous or hæmorrhagic necrotic nodes in the extremities (and elsewhere)

ERYTHEMA NODOSUM in the legs or forearms is too well known to warrant description (fig 2 13) It seems to be a non specific allergic type of tissue re action to a variety of antigenic agents including tuberculosis meningococcal

septicæmia streptococcal infection and a host of drugs particu on sulphathiazol It is not uncommon in sarcoidosis and is sometimes afeel ciated with rheumatic fever Not infrequently none of these agentoth relationships can be demonstrated with certainty



Fig 2 13—Typical distribution of erythema nodosum

RHEUMATIC NODULES are illustrated and discussed in Chapter IX Similar and larger nodules may occur in rheumatoid arthritis

Heberden s nodes and chalky deposits of gout have already been mentioned

SPIDER NÆVI are not nodes but may be mentioned here for convenience They are characteristic of advanced disease of the liver and are usuall as ociated with bright red palms and other evidence of vasodilatation (see Chapter XX)

A GLOMUS TUMOUR is a minute subcutaneous erythematous or bluish point *usually under a nail and often exquisitely painful It is mentioned* here because it may be mistaken for an Osler s node It is essentially a small innocent tumour of one of the rounded arterio venous shunt arrangements known as glomera (*glomus,* a ball) which are so numerous in the tips of the fingers and palms

Nervous disorders

MOIST PALMS provide good evidence of an anxiety state

TREMOR should be interpreted with care Thyrotoxic tremor is fine regular, and constant The tremor of an ar cuff was designed for an irregular and inconstant-d arm e tremorpplied to a large arm or thigh

...ins disseminated sclerosis, fatigue or senility occasionally it is con Congenital

CARPAL TETANY of the hands is commonly due to hysterical hyperventilation (1896) which causes tissue alkalæmia it is quickly relieved by the inhalation of in its rh on dioxide The sign is valuable when it is clinically uncertain whether thin erbreathing is due to pulmonary or cardiac disease or to hysteria A e g en ous tourniquet applied to the limb will augment carpal spasm (Trous defe u s sign) or tapping the facial nerve with the finger may cause an obvious e facial twitch (Chvostek's sign)

di PERIPHERAL NEURITIS with motor weakness impairment of sensation and loss of tendon jerks may give the clue to the nature of an obscure cardio pathy such as periarteritis beri beri and diphtheria The signs of neuro syphilis may disclose the cause of aortic incompetence or a mediastinal mass signs of subacute combined degeneration of the cord may at once explain a hyperkinetic circulatory state transient paraplegia immediately distinguishes dissecting aneurysm from coronary thrombosis evidence of poliomyelitis however slight may reveal the true nature of a myocarditis

Pigmentation

Brownish pigmentation of the skin may be due to Addison s disease hæmochromatosis or scleroderma

Loss of hair

Loss of axillary hair is characteristic of hæmochromatosis

A host of other signs may be found in the extremities but most of those which have a bearing on the cardiovascular system have been mentioned and underline the importance of examining the hands and feet very closely

THE BLOOD PRESSURE

The blood pressure was first measured directly in a live mare by Stephen Hales (1733) a brass pipe 1/6th of an inch in diameter was inserted into the left crural artery and connected to a vertical glass tube, blood rose in the tube to a height of 8 feet 3 inches above the level of the left ventricle

An excellent detailed account of the subsequent history of sphygmo manometry may be found in a monograph by Master Garfield and Walters (1952)

Technique of measurement

CLINICAL ESTIMATION Approximate estimation of the blood pressure by clinical means is not only possible but should be practised regularly, with experience it is easy to tell whether it is low normal or high and the procedure takes but a moment The physician should stand in front and to the right of the patient and should compress the right brachial artery description (fig 2 13) While feeling the right radial pulse with the fingers action to a variety of antigenic ...ed to obl... the pulse represents the

systolic blood pressure The alternative method of placing three fingers on the radial artery the first to compress the vessel above the second to feel the pulse and the third to obliterate the ulnar collateral below is both difficult and cumbersome

SPHYGMOMANOMETRY In cardiovascular work however the blood pressure should always be measured with a mercurial manometer or reliable aneroid instrument The patient must be comfortable whether lying or sitting and must have had time to recover from any recent excitement or exertion The arm should be bared to the shoulder to avoid constriction from clothing and to facilitate proper application of the cuff The latter should be fitted closely and evenly round the arm so that its lower edge is one inch above the bend of the elbow and the middle of the rubber bag lies over the brachial artery Preliminary readings should be taken by palpation the cuff is inflated rapidly until the brachial pulse is obliterated and is then deflated slowly the point at which the brachial pulse first reappears represents the systolic pressure as the cuff is further deflated brachial pulsation gradually assumes a water hammer quality and then abruptly resumes its normal character the reading corresponding to this sudden change represents the diastolic blood pressure When approaching an end point the pressure must be altered slowly in the cuff The palpatory method avoids the pitfall of the auscultatory gap and is uninfluenced by subjective auditory defects nevertheless it should be checked by auscultation The stethoscope should be applied lightly and accurately over the brachial artery just below but not in contact with the cuff The latter is then inflated to a pressure of some 30 mm Hg above the systolic pressure as found by palpation and slowly deflated The accepted systolic blood pressure is the highest level at which successive sounds (phase I of Korotkow) are heard As the pressure is further lowered in the cuff the dull thud of the upper limits is replaced first by a murmur (phase II of Korotkow) and then by louder and sharper sounds (phase III) the point at which these slapping sounds suddenly become muffled (phase IV) is usually taken as the diastolic pressure When there is vasodilatation especially when associated with aortic incompetence sounds may still be heard when the cuff pressure is reduced to zero but normally they disappear a few mm Hg below the change over

The above recommendations are freely borrowed from the joint report of the committees appointed by the British Cardiac Society and the American Heart Association for the standardisation of methods of measuring the arterial blood pressure (1939)

SIZE OF THE CUFF The cuff method of measuring the blood pressure is not entirely accurate Riva Rocci s cuff (1899) was only 4 5 cm wide and gave falsely high readings as shown by von Recklinghausen (1901) who introduced the standard 5 inch cuff (12 7 cm) During the last twenty years it has been pointed out repeatedly that this cuff was designed for an adult with an average sized arm when applied to a large arm or thigh the

reading obtained is too high, and when applied to a small arm the reading is too low (Ragan and Bordley 1941) For infants the cuff should not exceed 2.5 cm (Woodbury Robinow and Hamilton 1938) for young children it should be about 3 inches wide and for the outsized adult 7 or 8 inches wide Even with these precautions cuff readings only approximate those recorded directly by means of arterial puncture the systolic level averaging 8 mm Hg too low and the diastolic (taken at the point of muffling) 8 mm Hg too high (Bordley *et al* 1951) The point at which sounds cease altogether is actually nearer the true diastolic pressure and is gradually gaining favour on that account but it is technically a less satisfactory end point

AUSCULTATORY SILENT GAP—When there is hypertension sounds occasionally disappear as the cuff is inflated but reappear at higher levels In standing patients the gap is encouraged by allowing the arm to hang down and discouraged by elevating the arm (Berry 1940) Similarly the gap is favoured by inflating the cuff slowly and may be abolished by inflating it rapidly (Ragan and Bordley 1941) The phenomenon may be related to the development of a very high venous pressure distal to the cuff which causes the diastolic arterial pressure to rise well above its proper level thus diminishing the pulse pressure

IRREGULARITIES When there are ectopic beats the higher pressure of the beat that follows the ectopic should be ignored In auricular fibrillation only approximate readings can be obtained the systolic pressure should be taken at the point where the majority of beats come through the diastolic where the majority of beats become muffled As the blood pressure normally varies by a few mm Hg with respiration it may be suitably recorded to the nearest multiple of five

Normal range

THE NORMAL SYSTOLIC BLOOD PRESSURE lies between 95 and 150 mm Hg Whilst it is true that apparently normal subjects between the ages of 40 and 65 tend to have higher systolic pressures than those between 20 and 40 insurance companies well recognise the value of low figures and it is probable that the higher average pressures of the middle aged and elderly are due to atherosclerosis (Lewis 1938)

THE NORMAL DIASTOLIC BLOOD PRESSURE lies between 60 and 90 mm Hg The mean pressure approximates to the diastolic plus one third of the pulse pressure

Although these figures have been standard for a long time a det[illegible]ned attempt to raise the upper limits of normal has recently been [illegible]ade by Master Garfield and Walters (1952) In their well reasone[illegible]ograph these authors have made a strong plea for accepting a figu[illegible] 100 plus the age of the patient in years plus 5 to 10 mm Hg as [illegible] limit of normal systolic pressure for middle aged men (aged 40 [illegible]) and a figure 5 mm Hg higher for women between the ages of [illegible] They also

provided good evidence for raising the upper limit of the normal diastolic pressure from 95 to 100 mm Hg in men and women over 50 years of age

IN CHILDREN the blood pressure averages 90/60 between the ages of 3 and 9 95-100/60-65 between the ages of 10 and 12 and 105 65 between the ages of 13 and 15 (Judson and Nicholson 1914)

A COMMON SOURCE OF ERROR in blood pressure estimation results from failure to obtain a reasonably basal reading this may be due to impatience or to lack of recognition of emotional or other physiological factors When ever the pressure is found to be raised the cuff should be left in position so that a second reading may be taken at the end of the examination Casual measurements in healthy young adults who are a little anxious often register 160/90 mm Hg but if the patient is put at ease and allowed to rest quietly on a couch this figure may fall steadily to normal levels It must be thoroughly understood that the maximum normal blood pressure of 150/90 mm Hg is meant to be at ease The question of pre hypertensive levels will be discussed later

Slight *disparity between readings taken from each arm* is common especially in atherosclerotic and hypertensive subjects but the difference rarely exceeds 5 mm Hg (Amsterdam and Amsterdam 1943) The blood pressure is sometimes taken in the legs with the cuff above the knee and the stethoscope in the popliteal fossa In the average normal individual in the horizontal position *the blood pressure in the legs* reads 20 to 40 mm Hg above that in the arms The discrepancy is due to using the standard cuff as previously described, and is not found when records are obtained by means of direct arterial puncture (Loman *et al* 1936) *In the standing position* the systolic pressure in the arms measured at heart level usually shows no appreciable change but in 33 per cent of normal subjects it drops about 10 to 15 mm Hg the diastolic pressure rises about 5 mm Hg in 48 per cent of normal subjects drops about 5 mm Hg in 12 per cent and remains unchanged in 40 per cent (Currens 1948) *At death* all intra vascular pressures level out at 14 to 22 mm Hg This is known as the static pressure and may be reached during periods of prolonged asystole (Dowling *et al* 1952 Anderson 1954)

THE OCULAR FUNDI

Before leaving the peripheral vascular system the ocular fundi should be examined The ophthalmoscope should be used with both eyes open and with either hand so that one may hold the instrument with the right hand when examining the patient s right eye and with the left hand when examining his left eye There are four features of particular interest to the cardiologist the appearances of the disc the state of the arteries the presence of hæmorrhages and the presence of exudates

PAPILLŒDEMA may occur in acute or chronic renal hypertension and necessarily in malignant hypertension (by definition) In these cases swelling of the disc is usually attributed to the high cerebro spinal

pressure that is commonly found but it is by no means clear just why the C S F pressure should be raised. Papillœdema may also occur in anoxic cor pulmonale (see frontispiece) and here again the C S F pressure is high possibly because of increased filtration through the choroid plexus resulting from cerebral vasodilatation due to carbon dioxide retention Papillœdema is seen occasionally in bacterial endocarditis when it is usually associated with acute nephritis also in temporal arteritis and rarely in periarteritis nodosa When found in association with other kinds of cardio vascular disease cerebral tumour is more likely to be responsible It does not occur in congestive heart failure or in chronic constrictive pericarditis nor even in the majority of cases of superior vena cava obstruction despite jugular venous pressures up to 30 mm Hg and correspondingly high C S F pressures

THE CALIBRE OF THE RETINAL ARTERIES should be compared with that of the veins and expressed as an A/V ratio the normal being 4 5 or 5/5 It should be understood that only the blood stream flowing through the artery or vein is seen the wall of the vessel itself being normally invisible The lighter longitudinal band in the centre represents reflection of light from that part of the vessel which lies in a plane more or less at right angles to the beam from the ophthalmoscope The state of the arteries in hyper tension is described in Chapter XVI Here it may be added that both arteries and veins become very small in cases of optic atrophy that a thrombosed artery is represented by a white streak that remarkably large veins may be physiological and that vasodilatation causes venous rather than arterial pulsation (this is well seen in cases of aortic incompetence)

HÆMORRHAGES Retinal hæmorrhages are discussed in relation to hyper tension in Chapter XVI They may also occur in bacterial endocarditis, diabetes mellitus acute nephritis periarteritis nodosa disseminated lupus temporal arteritis and any condition which may give rise to petechiæ Extensive hæmorrhage may follow venous thrombosis Sometimes its cause is not apparent

EXUDATES Retinal exudates associated with hypertension are described in Chapter XVI Exudate may also occur in any of the conditions specified in the preceding paragraph

JUGULAR VENOUS PRESSURE

General considerations

The jugular venous pulse should be analysed clinically in terms of pressure and wave form it is hard to conceive of any physical sign that is more informative

It should first be understood that the mean intravascular pressure generated by left ventricular systole and maintained by aortic valve closure gradually falls as energy is expended overcoming the peripheral resistance so that from a level of about 90 mm Hg in the aorta and major arteries

it falls to around 70 mm Hg in the smallest arteries 30 mm Hg in the smallest arterioles about 10 mm Hg in the venules and around zero in the great veins When there is arteriolar vasodilatation the venous pressure tends to rise a little and when there is arteriolar vasoconstriction it tends to fall If the venous return from any part is totally obstructed the pressure in the veins distal to the obstruction rises rapidly to arterial level provided the arteries are not also obstructed The central venous pressure is also influenced by right atrial contraction and relaxation closure of the tricuspid valve right ventricular diastolic tone and the intrathoracic pressure (normally negative)

As seen at the bedside the jugular venous pulse is the oscillating top of the distended proximal portion of the internal jugular veins and represents volumetric changes which faithfully reflect the right atrial pressure at all stages of the cardiac cycle Thus if the mean pressure in the right atrium is 10 cm of water the jugular veins will be distended to an average point in the neck exactly 10 cm vertically above the centre of the right atrium (disregarding the specific gravity of blood which is 1 056) The veins above this level are collapsed for the actual pressure within them is less than atmospheric This introduces another facet of the subject which it may be as well to clarify at once The pressure at any given point in the circulation is always expressed in relation to a fixed geographical reference point usually the heart itself In the simple illustration just mentioned the actual pressure at the top of the jugular venous pulse is zero but if the base line of the manometric system is set at heart level the reading becomes 10 cm of water which represents the 10 cm height of water in the tube connecting the manometric base line to the needle in the vein Similarly the actual pressure in the inferior vena cava at a point 15 cm below heart level in the same illustration is 25 cm of water but the reading is still 10 in relation to heart level because the 15 cm column of water in the connecting tube exerts a negative pressure of 15 cm of water on the manometric system In this way the influence of gravity is removed from all pressure measurements a highly desirable condition because in a closed circuit such as the circulation the effects of gravity in the arterial and venous pressures are necessarily opposed and tend to cancel each other out in so much as the blood vessels do not behave like rigid tubes this annulment of the effects of gravity is far from perfect but natural adjustments normally compensate for the disparity

Recognition of venous pulsation

Venous pulsation in the neck can be recognised and distinguished from arterial pulsation in the following ways

1 The movement is soft diffuse and undulant

2 The pulse that is seen cannot usually be felt

3 With normal rate and rhythm there are two crests and two troughs per cardiac cycle

4 When timed against the carotid pulse only the first trough appears to coincide with systole This is the x descent which follows the presystolic a wave The second crest v appears to be late systolic or early diastolic and the second trough y is obviously diastolic (fig 2 14)

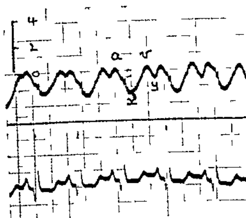


Fig 2 14—Normal central venous pulse recorded simultaneously with the electro cardiogram The x descent is interrupted by a small c wave or by a first heart sound artefact The rate of 116 beats per minute is too fast for the full development of y

5 The top level of pulsation normally drops to a lower level on inspiration and rises to a higher level on expiration passively following the changes in intrathoracic pressure

6 The jugular venous pressure usually rises on abdominal compression This may increase the intrathoracic pressure or raise the total intra abdominal venous pressure and it matters little to what part of the abdomen pressure is applied (fig 2 15)



Fig 2 15—Rise of venous pressure on abdominal compression compressing the left iliac fossa is as effective as compressing the liver (Time marking 1 mm per sec)

7 The jugular venous pressure varies with posture being higher in the horizontal position and lower in the vertical owing to the influence of gravity

8 Cervical venous pulsation ceases if the jugular veins are compressed at the root of the neck

9 Light pressure of the finger against the root of the external jugular vein distends the upper part of the vessel On removing the finger the vein collapses to the level of the mean jugular venous pressure

Clinical measurement of jugular venous pressure

The most satisfactory reference point from which to measure the jugular venous pressure is the sternal angle Lewis chose this point because its relation to the right atrium is more or less stable being about 5 cm above the centre of the right atrium in both the horizontal and vertical positions The patient should be propped up at 30 60 or 90 degrees whichever position reveals maximum venous pulsation The vertical distance between the top of the oscillating venous column and the sternal angle represents the central venous pressure and is recorded in centimetres (of blood) above the sternal angle The incline of the patient when the measurement was made should also be recorded because the venous pressure varies with posture as previously stated (this has nothing to do with the relationship of the sternal angle to the right atrium)

The *normal jugular venous pressure* ranges between plus 3 cm and about minus 7 cm with reference to the sternal angle with the patient horizontal The mean right atrial pressure averaged minus 1 5 mm Hg with reference to the sternal angle in 50 normal controls studied by the author

Causes of an elevated venous pressure

The venous pressure may rise under a variety of physiological and pathological conditions in addition to heart failure

1 *Physical effort* raises the venous pressure owing partly to the squeezing action of skeletal muscular contraction on the veins and partly to peripheral vasodilatation the effect may be masked by reduction of the mean intrathoracic pressure resulting from hyperventilation The venous pressure rises sharply during a rigor

2 *Hyperkinetic circulatory states* due to heat fever pregnancy anæmia arterio venous aneurysm beri beri thyrotoxicosis Paget s disease of bone hypoxia or advanced disease of the liver are all associated with a rise of venous pressure which may be partly attributed to vasodilatation The cardiac output is raised and it may be difficult to be sure whether the heart is overloaded or not Amyl nitrite acetyl beta methylcholine and other vasodilators in therapeutic doses may have a similar effect

3 *An increased blood volume* is usually due to sodium retention and occurs physiologically in women during the pre menstrual phase and in

pregnancy it occurs pathologically in acute nephritis without denoting heart failure and can be induced artificially by feeding with salt and desoxycorticosterone acetate by pitressin A C T H therapy and of course by large intravenous infusions

4 *A sufficiently slow heart rate* whether due to heart block or not is usually associated with a rise of venous pressure owing to right ventricular resistance to overfilling To maintain an adequate cardiac output per minute the stroke output may have to be doubled Thus a rise of venous pressure does not necessarily mean congestive failure in cases of complete heart block

5 *An increased intrathoracic pressure* raises the jugular venous pressure but not the right ventricular filling pressure The effect is produced momentarily during the act of coughing and artificially by means of the Valsalva manœuvre Pleural effusion may have a similar effect and may be wrongly attributed to heart failure in consequence

6 *An increased intra abdominal pressure* probably acts indirectly by raising the intrathoracic pressure Tight corsets abdominal binders trousers too tight round the waist, obesity alone ascites pregnancy or even gross flatulence may each have this effect To witness alleged heart failure immediately relieved by undoing the top trouser buttons can be both embarrassing and instructive

7 *A raised intrapericardial pressure* from effusion increases the filling resistance of the right ventricle and so raises the jugular venous pressure Chronic constrictive pericarditis has the same effect

8 *Partial obstruction of the superior vena cava* raises the jugular venous pressure without abolishing pulsation only when the block is complete or very nearly so does venous pulsation cease *Obstruction of the inferior vena cava* may raise the jugular venous pressure indirectly by interfering with renal function and sodium excretion

9 *In tricuspid stenosis* the raised venous pressure is associated with a normal right ventricular diastolic pressure

10 *Space filling lesions affecting the right side of the heart* prevent proper filling of the right ventricle and include massive thrombosis of the right atrium tumour, constrictive endocarditis aneurysm of the interventricular septum and Bernheim s syndrome

11 *Giant a waves cannon waves* and *tricuspid incompetence* raise the jugular venous pressure during a particular phase of the cardiac cycle and will be considered in relation to the venous pulse (*vide infra*)

12 *Congestive heart failure* itself of course is the most important cause of an elevated venous pressure and is discussed in detail in Chapter VII hydræmia from sodium retention resistance to right ventricular over-

filling and sometimes functional tricuspid incompetence are all implicated

In all the pathological conditions mentioned above (apart from coughing and the Valsalva manœuvre) venous pulsation is preserved and with the exception of partial S V C obstruction the jugular venous pressure represents the right atrial pressure When the cervical veins are distended but do not pulsate, they are either obstructed at the root of the neck or there is total obstruction of the superior vena cava Obstruction of one or more cervical veins at the root of the neck may be due to kinking or local compression from neighbouring structures and may disappear at once if the relationship between the head and neck and the shoulder girdle is altered

Therapeutic methods of raising the central venous pressure include the horizontal posture (more effective if the legs are raised) leg binders exerting a subarterial pressure on as large a surface as possible from the toes to the hips overalls that can be inflated to any desired pressure intravenous infusions and salt with desoxycorticosterone Selective chemical venoconstrictors have not yet been discovered Arteriolar vasodilators are usually contra indicated because the blood pressure is too low in these cases and there is already too much blood laked in the periphery moreover many such substances are also venodilators

Venous pressure lowering agents include the erect or semi erect posture (sitting or propped up with the legs hanging down) venous tourniquets applied to the thighs venesection dehydration by means of sodium depletion (low sodium diet kation exchange resins carbonic anhydrase inhibitors and mercurial diuretics) and chemical venodilators such as theophylline tetraethylammonium and hexamethonium

THE JUGULAR VENOUS PULSE

Precise analysis of the cervical venous pulse and measurement of the height of each individual wave with reference to the sternal angle is not only possible at the bedside but highly desirable In the previous section on the jugular venous pressure there was a noticeable lack of precision concerning the wave responsible for the pressure actually measured this defect will now be remedied

Definition of waves

The jugular venous pulse consists essentially of four waves *a x v* and *y* (fig 2.16) The first and third waves (*a* and *v*) are crests the second and fourth (*x* and *y*) troughs A fifth wave known as *c* another crest, may interrupt the *x* descent and a final upward movement often quite sharp follows *y* There is some advantage in allotting the letter *z* to the point reached by this last movement before the inscription of the *a* wave of the next cardiac cycle

The a wave is due to right atrial systole and disappears in auricular fibrillation

The x descent is due chiefly to atrial relaxation and also disappears in

auricular fibrillation (fig 2 17) for this reason it is difficult to believe that withdrawal of the atrioventricular septum towards the cavity of the right ventricle a movement known as descent of the base is mainly responsible for x

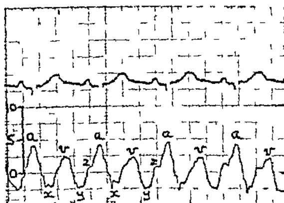


Fig 2 16—Normal right atrial pressure tracing c is represented by a small notch towards the end of the x descent the rise of pressure from the trough y to the zero point z before atrial contraction is well shown

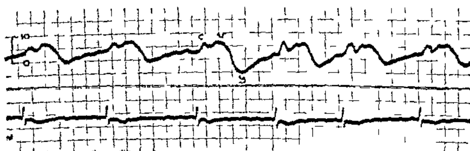


Fig 2 17—Pressure pulse from the right atrium in a case of mitral stenosis with auricular fibrillation showing absence of the x descent

The c wave which may interrupt the *x* descent was first attributed to tricuspid valve close (Potain 1867) and later to a carotid artefact (Mackenzie 1902) While admitting that a *c* wave due to mitral valve closure is usually prominent in direct left atrial pressure tracings in cases of mitral stenosis (fig 2 18) the writer has found relatively few conspicuous *c* waves due to tricuspid valve closure in well over a thousand right atrial pressure tracings obtained from a wide variety of cases including 50 normal subjects There is a great deal of difference between the forceful closure of the mitral valve in mitral stenosis and the gentle apposition of the tricuspid leaflets in normal hearts Clinically *c* is unobtrusive in the majority of

jugular venous pulses the trough x usually accompanying the early part of systole in cases with normal rhythm (figs 2 14 and 2 16) The *c* wave of external jugular phlebograms is always far more prominent (fig 2 19) and as shown by Mackenzie represents the carotid pulse itself

There is some evidence that well defined *c* waves due to tricuspid valve closure may occur in atrial septal defect and they might be expected in any condition in which the tricuspid valve is wide open at the moment the ventricle contracts

The v *wave* represents a rising right atrial pressure due to temporary obstruction of the blood flow during ventricular systole When there is

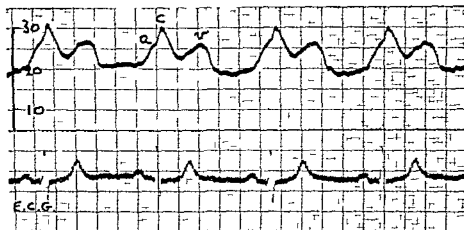


Fig 2 18—Left atrial pressure tracing showing a powerful *c* wave closely following *a* in a case of mitral stenosis

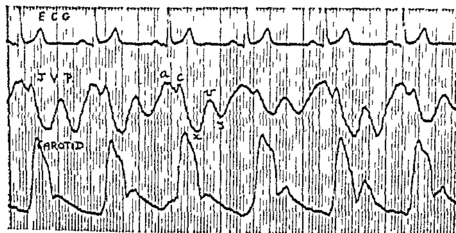


Fig 2 19—Conspicuous *c* wave in an external jugular phlebogram recorded simultaneously with the carotid pulse (see text)

normal rhythm it appears in late systole for it is at first overpowered by the x descent of atrial relaxation when there is auricular fibrillation however it starts with the first heart sound and occupies the whole of systole (fig 2 17)

The y descent begins as soon as the tricuspid valve opens i e at the end of the period of isometric ventricular relaxation This of course is the down slope of *v* just as the *x* descent is the down slope of *a* As the tricuspid valve opens there is a potential pressure gradient between the slightly raised right atrial pressure and the rapidly falling right ventricular pressure but they equalise rapidly and appear to fall together to the trough *y*

Return of pressure to the point z is gradual or rapid according to the ease with which the right ventricle dilates In normal hearts the ascent is gradual for there is little resistance to right ventricular filling

Normal venous pulse

The normal jugular venous pulse oscillates gently around a mean level a little below zero with reference to the sternal angle Typical figures for *a x v y* and *z* are o −4 o −3 ←1 mm Hg respectively *a* and *v* being about equal in amplitude, and the greatest excursion being the x descent Only with heart rates below 90 beats per minute is there time for full inscription of all five waves With heart rates between 90 and 110 the zero point is not defined *a* succeeding *y* immediately With rates higher than 110 there is no time for the proper development of *y* *a* succeeding *v* just as the *y* descent starts and at a rate of around 150 *v* and *a* are wholly superimposed These figures are only approximate for they vary considerably according to the length of the P R interval and the duration of ventricular systole

Clinically it is usually easy to measure the height of *a* and *v* in centimetres above the sternal angle and *z* is not difficult with slow rates but the troughs *x* and *y* may have to be estimated only approximately In clinical notes the form of the venous pulse should be drawn and a figure representing the approximate pressure of each wave should be inscribed in the appropriate place

Abnormalities of the jugular venous pulse

A giant a wave (fig 2 20) measuring between 6 and 15 mm Hg above *v* is characteristic of severe pulmonary hypertension severe pulmonary stenosis tricuspid stenosis or tricuspid atresia (provided there is no free right to left shunt in any of them) It is presystolic abrupt and collapsing in quality (venous Corrigan) palpable transmitted to the liver and usually associated with right atrial gallop and a conspicuous P pulmonale It alters little if at all with change of posture and increases in amplitude both with inspiration (fig 2 21) and abdominal compression The powerful right atrial contraction responsible for the giant *a* wave seems to be due to increased resistance to right ventricular filling over a long period of time

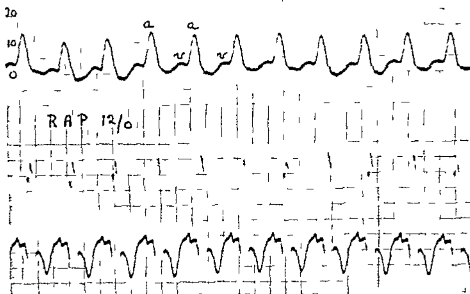


Fig 20—Giant *a* wave in pulmonary valve stenosis with reversed interatrial shunt

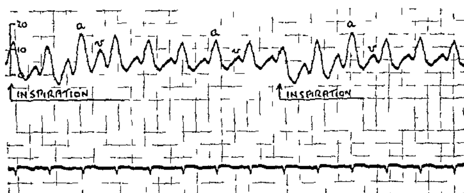


Fig 2 1—The effect of respiration on the giant *a* wave

It does not occur in ordinary cases of heart failure in which the right ventricular diastolic pressure is raised and it is usually absent in both Eisenmenger s complex and Fallot s tetralogy Teleologically in pulmonary hypertension and pulmonary stenosis it serves to increase the contractile force of the right ventricle in accordance with Starling s law which states that within certain limits the force of cardiac contraction is a function of fibre length When nodal rhythm has occurred fortuitously during cardiac catheterisation in several of these cases the right ventricular systolic pressure has fallen abruptly by 20 to 30 mm Hg (fig 2 22)

A prolonged a c *interval* occurs in partial heart block Clinically the interval between *a* and the carotid pulse can be graded easily enough into

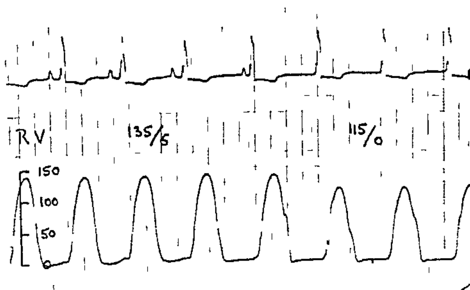


Fig 2 22—Right ventricular pressure tracing from a case of severe pulmonary valve stenosis showing a sudden fall in pressure of at least 20 mm Hg with the onset of nodal rhythm (see text)

short (P R interval around 0 12 sec) average (P R 0 16 sec) rather long (P-R 0 20 sec) and obviously prolonged (P R 0 24 sec) When P R is longer than 0 24 second *a* tends to fuse with *c* as it does with sinus tachycardia and normal conduction

Independent a *waves* occur in complete heart block They are usually of small amplitude and likely to be overlooked unless the venous pulse is studied very carefully

Cannon waves are more obvious and occur whenever the right atrium contracts against a closed tricuspid valve i e when the P wave of the electrocardiogram falls between the end of QRS and the end of T This occurs irregularly in complete heart block (fig 2 23) and with multiple ectopic beats and regularly with nodal rhythm paroxysmal nodal tachycardia and partial heart block with an extremely long P R interval

A cannon wave is *not* a summation effect but a particular form of giant *a* The whole of the energy released by right atrial contraction is translated into pressure because forward flow is impossible The word is used in the sense of rebound apt enough since the tricuspid valve is shut in the face of the oncoming wave from the atrium

In complete heart block cannon waves are *not* synchronous with cannon sounds on the contrary the first heart sound associated with a cannon wave is relatively quiet The cannon sound in heart block refers to the explosive first sound that is heard when the atria contract about 0 10 second before the ventricles so that the mitral cusps flung wide open by atrial contraction are slammed shut by the quickly succeeding ventricular systole —another kind of rebound altogether if the word is still used in that sense

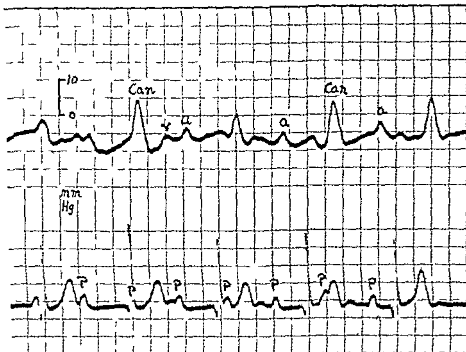


Fig 2 23—Irregular cannon waves in the central venous pulse in a case of complete heart block cannons are seen whenever P falls between Q and the peak of T in the electro cardiogram

In 2 1 heart block alternate *a* waves usually broaden x and are incon spicuous but if they fall a little earlier regular cannon waves may be observed

Ectopic beats may cause cannon waves in several different ways An atrial ectopic may coincide with the previous ventricular systole Nodal ectopics usually cause the atria and ventricles to beat together as in nodal rhythm Ventricular ectopics cause cannon waves when they are only slightly premature so that they coincide with normal atrial contraction excited by discharge of the sinus node

Paroxysmal tachycardia need not necessarily be nodal to cause cannon waves Atrial tachycardia may do so when there is 2 1 fatigue block (if atrial contraction is forceful enough) or when P R is prolonged so that P falls before the end of the preceding T wave and ventricular tachycardia may cause irregular cannon waves when atrial contraction is independent

Absence of a conspicuous x descent is invariable in auricular fibrillation instead there is a broad positive systolic wave x sometimes initiated by a small *c* wave (fig 2 17) If the x descent were due chiefly to downward movement of the atrial floor during ventricular systole it should be influenced but little by auricular fibrillation

The *x* descent is diminished in tricuspid incompetence but may still be recognised when the rhythm is normal (fig 2 24) The x descent is similarly

absent from direct and indirect left atrial pressure pulses in cases of auricular fibrillation but may be present in mitral incompetence when the rhythm is normal

Large v waves are especially characteristic of tricuspid incompetence with auricular fibrillation (fig 2 25) and are transmitted to the liver The

Fig 2 24—Case of tricuspid valve disease (due to lupus) with stenosis and incompetence and with normal rhythm showing an *x* descent before the v wave The bottom tracing is a continuous record of the pressures obtained as the catheter was withdrawn from the pulmonary artery (left) to the right atrium (right) note the pressure gradient across the tricuspid valve



Fig 2 25—Case of tricuspid incompetence with auricular fibrillation showing a large v wave

high amplitude of the systolic wave is augmented by the deep y trough which follows

A deep y descent or diastolic collapse of the venous pulse was first described in relation to chronic constrictive pericarditis (Friedreich 1864) In these cases the venous pressure is high throughout the cardiac cycle except for a short period immediately following the opening of the tricuspid valve when blood from the right atrium pours into the relaxing right ventricle Right atrial and ventricular pressures equalise rapidly and the small cavity of the right ventricle is quickly filled further filling is resisted by the rigid pericardium so the pressure rises again sharply during the rest of diastole (fig 2 26)

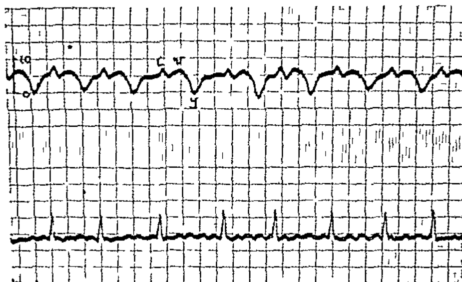


Fig 2 26—The steep y descent in a case of Pick s disease

It was at first thought that the rigid pericardium tensed inwards during systole (either alone or in conjunction with the chest wall) recoiled like a spring in early diastole and so created a powerful negative pressure which explained the diastolic venous collapse but although such a mechanism may exist it is superfluous to the thesis for the same phenomenon occurs in any condition in which the venous pressure is very high provided there is no obstruction at the tricuspid valve (fig 2 27) In severe right ventricular failure for example the same high potential pressure gradient between atrium and ventricle must exist immediately the tricuspid valve opens ventricular filling and equalisation of pressures are just as rapid and further filling is resisted by the already overstretched fibres of the failing myocardium the stroke output in these cases is just as small as in Pick s disease

Fig 2 27—Jugular phlebogram showing a steep y descent and deep x trough in a case of mitral stenosis with extreme pulmonary hypertension

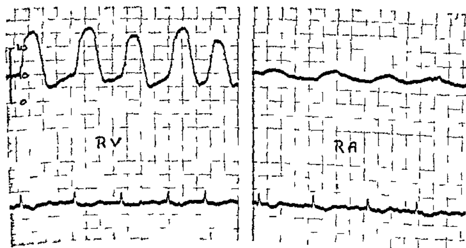


Fig 2 28—Case of tricuspid stenosis showing a slow y descent

A slow y descent following *v* despite a high venous pressure is characteristic of tricuspid stenosis (fig 2 28), for rapid equalisation of jugular and right ventricular pressures is then impossible The same sluggish *y* descent is seen in left atrial pressure tracings in cases of mitral stenosis (Owen and Wood 1955) Again in tricuspid stenosis there is no rapid rise of pressure following the *y* trough as there is in heart failure and Pick s disease so that *z* is little if at all higher than *y*

OTHER CLASSICAL SIGNS OF HEART FAILURE

If the jugular venous pressure is raised in a manner suggesting heart failure a *distended and often tender liver* can usually be palpated If the liver edge cannot be felt the epigastrium and right hypochondrium should be percussed a good resonant note up to the right costal margin anteriorly excludes significant enlargement A high venous pressure without hepatic enlargement suggests obstruction of the superior vena cava enlargement of the liver without a rise of venous pressure should never be attributed to heart failure

Œdema does not necessarily accompany a raised venous pressure due to heart failure as explained in Chapter I on the other hand cardiac œdema does not occur without a raised venous pressure The swelling is maximal round the ankles in ambulant patients but may be chiefly sacral in those confined to bed Its mechanism is discussed in Chapters I and VII

Physical signs of pulmonary venous congestion due to left ventricular failure are usually wanting Basal rales are notoriously unreliable being absent in the majority of cases and often having another interpretation when present In acute pulmonary œdema however fine crepitations can be heard over a wide area of both lungs The explanation for these two statements is simple enough a rise of pulmonary venous pressure up to 30 mg Hg causes no exudation of serum into the alveoli and therefore does not give rise to crepitations only when the pulmonary venous pressure exceeds the osmotic pressure of the plasma does such exudation occur i e in acute pulmonary œdema When basal rales are heard in either left ventricular failure or mitral stenosis in the absence of pulmonary œdema increased bronchial secretions are culpable but although pulmonary venous congestion may be responsible for the increased bronchial activity the sign is so common in simple bronchitis or bronchiolitis that it cannot be accepted as reliable evidence of heart failure

EXAMINATION OF THE HEART

Having gleaned as much information as
from examining the peripheral vascular s
from searching for signs of failure one may
heart itself and duly inspect palpate pe

Inspection

The position and character of the cardiac impulse if visible and of any other thoracic pulsation should be noted In this way left or right ventricular hypertrophy, gallop rhythm dilatation of the pulmonary artery and aortic aneurysm may be detected Præcordial deformity may be observed and if due to the heart indicates its enlargement during the period of thoracic growth Depression of the sternum or other thoracic deformity should be noted for it may alter the shape or position of the heart Systolic indrawing of the thoracic wall is not abnormal if it occurs over the right ventricle and is exaggerated in this situation when the left ventricle is alone enlarged and it may be seen in the anterior axillary line or beyond when there is gross enlargement of the right ventricle As a sign of adherent pericardium it should be looked for posteriorly over the last two ribs as described by Broadbent (1895)

Palpation

The apex beat which is a geographical point should be determined by locating the exact site of the left ventricular impulse The physician s hand should be placed over the region of the fifth left intercostal space in the nipple line in order to ascertain its approximate position the middle finger should then be directed vertically over it and shifted about until the maximum thrust is located This, rather than the lowest left point of such pulsation, is the apex beat Its position should be recorded with reference to the intercostal spaces to the mid line and to the mid clavicular line If it is located beyond these confines the possibility of displacement from scoliosis elevation of the diaphragm or from pulmonary or pleural lesions should be considered before concluding that the heart is enlarged

The character of the cardiac impulse is as important if not more important than its position (the apex beat) it should be sensed both with the palm of the hand and with the finger tip A steady heaving impulse means left ventricular hypertrophy and is felt in aortic stenosis and systemic hypertension A hyperdynamic impulse is also forceful but has greater amplitude and is more abrupt and lively it signifies an overfilled ventricle usually working against a low resistance as in aortic incompetence mitral incompetence patent ductus ventricular septal defect and the hyperkinetic circulatory states Both heaving and hyperdynamic left ventricular impulses are usually associated with increased retraction of the chest wall overlying the right ventricle slight retraction in this region being normal A steady heave over the right ventricle about the left parasternal line is felt in pulmonary hypertension and pulmonary stenosis A hyperdynamic right ventricular lift is more tumultuous and is characteristic of the overfilled right ventricle of atrial septal defect A strong impulse over the right ventricle is usually associated with conspicuous retraction further to the left where the apex beat (left ventricular impulse) might have been expected This rocking movement is very easily seen and is the reverse

of the left ventricular rock described above When the left ventricle is small or rotated posteriorly and the right ventricle unimpressive no cardiac impulse may be felt at all only the tap of the first heart sound being appreciated this is typical of uncomplicated mitral stenosis when the first heart sound is accentuated

Palpation of the heart sounds in general can hardly be avoided not only the first but also systolic ejection clicks both elements of the second sound the opening snap of mitral stenosis the third sound and any kind of gallop are all frequently palpable when present

Palpation may next be used to detect the presence of thrills preferably in forced expiratory apnœa This manœuvre brings the heart and great vessels closer to the chest wall encourages the lung to retract from its buffering position and lessens the chance of confusing cardiac with respiratory phenomena Tricuspid thrills alone are better appreciated during inspiration The vibration sense of normal individuals varies considerably, but increased perception comes with experience and good technique

Practically all important murmurs, including certain functional murmurs may be accompanied by a thrill Indeed, of the twenty one different types of murmur described later in this chapter only the Carey Coombs murmur of active rheumatic carditis and the cardio respiratory murmur are never so accompanied

Percussion

The value of percussing the heart has given rise to much dispute man modern cardiologists maintaining that its place has been taken by the far more accurate and fertile method of radiography The older school how ever modestly suggest that it is a useful bedside method which give reliable and helpful information if practised diligently and if its limitation are appreciated Certainly if a fluoroscope is available percussion is poin less but a fluoroscope may not be available or the patient may be so i that only a portable X ray machine can be used and the distorted skiagram so obtained is liable to gross misinterpretation In such cases percussion may be of value and by constant practice the physician should learn wh it can and what cannot be expected from it

The approximate position of the left border of the heart may be checked when the apex beat is difficult to locate and dullness beyond the known or probable confines of the apex beat may sometimes be detected in cases of pericardial effusion

It is impossible to determine the right border of the heart by percussion unless there is aneurysmal dilatation of the right atrium On the o hand pericardial effusion even of moderate degree can often be dem strated

It was once customary to speak of relative and absolute cardiac dullness the latter being the note heard over the area of heart not covered by lung

but it is doubtful whether this distinction can be maintained Diminution or absence of cardiac dullness however is a useful sign of emphysema

Percussion at the base may be rewarded in pericardial effusion, there being characteristic dullness in the second left interchondral space when the patient lies flat also in substernal goitre and in anterior aneurysm of the aorta when a band of dullness extends laterally from the manubrium sterni

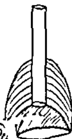
AUSCULTATION

When a man buys a tool for some specific purpose he usually takes care that it is the best available for the particular job in hand It is therefore strange that a superstition has grown up within the medical world that the older and more disreputable a stethoscope the better that it is not the stethoscope which matters but the man behind it This of course is nonsense When a student fails to hear a murmur which is heard easily by another exchange of stethoscopes quickly leads to mutual understanding

There is another curious tradition fostered by many who appreciate the value of a good stethoscope that the chest piece must be bell shaped and that any other type especially the flat diaphragm (Bowles) is pernicious This doctrine is as unreasonable as the first for there is no doubt that certain high pitched sounds especially aortic diastolic murmurs and faint tubular breathing which can be heard with ease through a Bowles may be inaudible through a bell The physical laws which govern auscultation have been studied by Rappaport and Sprague (1941 and 1951) The diameter of the Bowles chest piece should be about 1½ inches the cup should be shallow and its edge sharp (fig 2 29a) Good material for the diaphragm is photographic or X ray film washed clean in hot water, and cut to shape The rubber tubing should be thick about 10 inches long and should fit snugly to the connections The internal calibre of the whole system including the metal binaurals and the hole in the centre of the chest piece should be one eighth of an inch A good bell stethoscope (fig 2 29 b) is better for detecting low pitched sounds such as soft mitral diastolic murmurs more over its range of sensitivity may be increased by varying the force with which it is applied to the chest wall Light contact accentuates low pitched sounds firm pressure high pitched sounds The cup should not be too deep and its diameter not less than one inch



(a) Bowles



b) Bell

2 29—Binaural stethoscopes

There are two other types of stethoscope which deserve comment the monaural wooden instrument of by gone days and

the differential stethoscope (symballophone) The rigid wooden stethoscope is rarely used nowadays but by combining aural and tactile senses it facilitates the recognition of gallop rhythm The differential stethoscope is constructed as shown in figure 2 30 and may be used to compare the timing of sounds originating at different sites and to determine the direction in which a murmur is propagated (Kerr *et al* 1937)

Auscultation of the heart can only be learned at the bedside but the following advice may be helpful to students The præcordium should be examined all over not just at areas where individual valve sounds are expected gallop rhythm pericardial friction and certain important murmurs will not then escape notice It is enough to listen to one thing at a time thus when an expert hears a soft elusive mitral diastolic murmur hitherto overlooked it is not necessarily because he has better ears or a better stethoscope, but because he has acquired a more selective power of concentration Basal murmurs and pericardial friction are heard most easily in expiratory apnœa tricuspid murmurs during inspiration mitral murmurs in the left lateral position especially when the heart slows down after exercise Heart sounds should be timed against carotid pulsation if difficulty is experienced due to tachycardia the heart may be slowed by carotid sinus compression

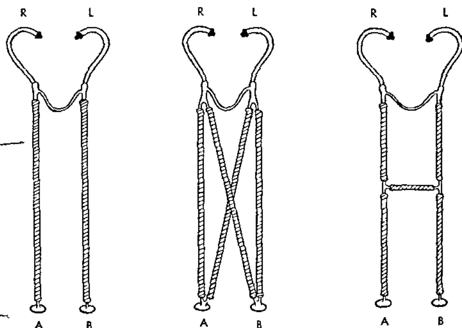


Fig 2 30—The differential stethoscope (3 varieties) Sounds travelling from A to B reach the right ear before the left giving the impression of movement in that direction

(Leatham and Vogelpoel 1954) they are also best heard in the third left space at the sternal edge but are not transmitted to the apex beat

If the definition of the first heart sound is extended to include vascular vibrations occurring at the end of the isometric contraction phase (Braun Menendez 1938) then an ejection click may be regarded as the second component of a widely split first sound There is an obvious advantage, however, in using the term aortic or pulmonary ejection click to describe this vascular sound and restricting the term split first sound to mean separation of mitral and tricuspid components only

The second heart sound is due to aortic and pulmonary valve closure The aortic element is heard best in the aortic area in the neck and at the apex beat and the pulmonary element in the pulmonary area In normal individuals both elements can usually be heard in the second and third left interchondral spaces close to the sternal border In children and adolescents the split is often obvious (grade II) particularly towards the end of inspiration The first element is aortic, the second pulmonary The lag of P2 during inspiration has been attributed to prolongation of right ventricular systole from increased filling (Leatham 1954) In atrial septal defect the split fails to widen on inspiration

Pathological splitting (grade III) is due to delay in pulmonary valve closure and is usually due to right bundle branch block delay in the emptying time of an overfilled right ventricle, or pulmonary stenosis In these cases the split may approach 0 1 second in width (grade I=0 02–0 03 sec grade II=0 04–0 05 sec) Slight delay in aortic valve closure may bring the two elements together and so cause a single second heart sound In aortic stenosis and left bundle branch block the aortic element may lag behind the pulmonary element a reversed split so caused tends to close on inspiration and widen on expiration and can thus be recognised by its paradoxical behaviour (Leatham 1954)

Recognition of a split second heart sound at once proves that both semilunar valves are functioning and thus excludes persistent truncus arteriosus pulmonary atresia and severe pulmonary stenosis although a very faint and delayed P2 can sometimes be heard in the last When the split is wide the intensity of the pulmonary element helps to distinguish pulmonary stenosis (P quiet) from right bundle branch block or atrial septal defect (P normal or rather loud) [4]

Accentuation of the second heart sound may result from systemic or pulmonary hypertension the clinical circumstances and the site of maximal intensity may decide which but sometimes it is only possible to be sure if there is sufficient splitting If the ascending aorta or pulmonary artery is unusually close to the anterior surface of the chest either because it is abnormal or because it is scantily covered by lung and chest wall the second heart sound is also loud Conversely *a soft or absent second heart sound* is usual in emphysema

About midway between the second and third heart sounds or about

0 08–0 1 second after A may be heard the *opening snap of mitral stenosis* (fig 2 31e) the sharp extra sound is due to the abrupt flapping back of the mitral cusps at the end of the period of isometric relaxation i e when the rapidly falling left ventricular pressure drops below the raised left atrial pressure The opening snap is best heard in expiration at the lower left sternal edge over the root of the aorta and over the left ventricle at the apex beat It is discussed more fully in relation to mitral valve disease in Chapter X

The physiological third heart sound (fig 2 31f) was well described by Gibson (1907) It is soft low pitched and often accompanied by a palpable shock it is more or less localised to the apex beat varies in intensity with respiration and is accentuated when the subject lies on the left side It may be heard in the great majority of children in about 50 per cent of young adults, occasionally in the middle aged and rarely in the elderly Phonocardiography shows that the third sound coincides with the latter half of the descending limb of the v wave of the jugular phlebogram i e with the end of the period of rapid ventricular filling (Ohm 1913) it is attributed to sudden distension of the left ventricle at this time (about 0 15 sec after the onset of A)

The third heart sound is accentuated by any condition which encourages rapid left ventricular filling e g mitral incompetence ventricular septal defect patent ductus Pick s disease the hyperkinetic circulatory states and left ventricular failure In the last of these examples the triple rhythm produced by the development of the third heart sound is called diastolic gallop and will be discussed more fully in Chapter VII

MURMURS

There are at least twenty different heart murmurs which can be recog nised by means of simple auscultation

1 *The apical presystolic murmur of mitral stenosis* (fig 2 32a) This is a left atrial systolic murmur left atrial contraction increasing the blood flow through the narrow mitral orifice towards the end of diastole It sounds crescendo especially when it suddenly augments a fading diastolic rumble and ends abruptly with an accentuated first heart sound but is not neces sarily so The murmur is best heard with the bell stethoscope when the patient lies on the left side and is often accompanied by a thrill

2 *The presystolic murmur of Austin Flint* (1862 1886) may be heard in any form of well developed aortic incompetence and is generally believed to be due to vibrations of the anterior (aortic) cusp of the mitral valve which is agitated by *the opposing forces of aortic reflux and left atrial contraction* (Da Costa 1908) It is indistinguishable in quality and timing from the presystolic murmur of mitral stenosis Phonocardiograms have confirmed the reality of the murmur in cases which have been proved later to have normal mitral valves at necropsy (Currens *et al* 1953)

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3 *The presystolic murmur of tricuspid stenosis* is similar in quality timing and mechanism to its mitral counterpart but is heard at the tricuspid area instead of at the apex beat and is appreciably louder during inspiration

4 *The apical pansystolic murmur of mitral incompetence* (fig 2 32b) This begins early immediately after the first heart sound as soon as the pressure

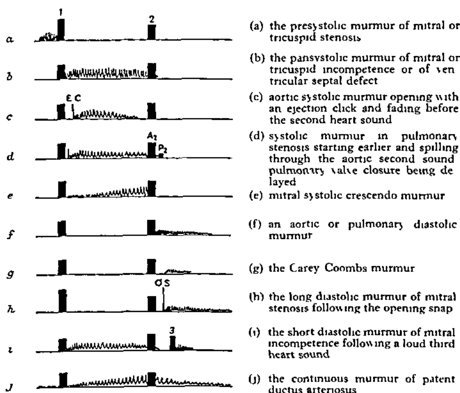


Fig 2 3 —The chief murmurs

in the left ventricle rises above that in the left atrium It also ends late embracing the aortic element of the second sound for the left ventricular pressure is still well above that in the left atrium when the aortic valve closes A thrill is common in organic cases but rare when the leak is functional

5 *The pansystolic murmur of tricuspid incompetence* is similar to its mitral counterpart except that it is heard best in the tricuspid area and is much louder during inspiration

6 *The pansystolic murmur of ventricular septal defect* (Roger 1879) is very like the murmur of mitral (or tricuspid) incompetence in quality and timing for the ordinary relationship between left and right ventricular pressure is not very greatly different from the relationship between left ventricular and left atrial pressure The murmur is heard best however

in the third and fourth intercostal spaces at the left sternal edge and is not accentuated by inspiration A thrill can be felt in 90 per cent of cases

7 *The aortic systolic murmur* (fig 2 32c) This is heard over the carotids in the aortic area in the third left intercostal space at the sternal edge and at the apex beat It does not begin with the first heart sound proper but after a short interval when the aortic valve opens an interval which becomes obvious enough when an aortic ejection click signals the opening of the valve The murmur is also relatively short ending just before aortic valve closure Turbulence may be due to increased flow as in the hyper kinetic circulatory states to dilatation of the ascending aorta or to aortic valve disease—especially stenosis An aortic systolic thrill usually means stenosis but may occur exceptionally with the other conditions mentioned

8 *The pulmonary systolic murmur* (fig 2 32d) This is more or less con fined to the pulmonary area and third left intercostal space at the sternal edge but may be much lower when the turbulence is infundibular It also begins a little while after the first heart sound proper its onset coinciding with the pulmonary ejection click when that is present i e with the opening of the pulmonary valve at the end of the period of isometric contraction It usually lasts longer than the aortic systolic murmur, for the pulmonary valve shuts later than the aortic Turbulence may be due to increased flow as in atrial septal defect to dilatation of the pulmonary artery or to pul monary or infundibular stenosis A thrill is nearly always present when there is stenosis but is by no means rare in uncomplicated A S D

9 *The crescendo mitral systolic murmur* (fig 2 32e) To the human ear this seems to begin rather late in systole and waxes greatly to end abruptly with the second heart sound just when it has reached its maximum It is usually due to trivial mitral incompetence although some authorities have stated it is commonly innocent (Evans 1948) Just how its curious crescendo quality is produced is unknown

10 *The late basal or posterior systolic murmur of coarctation of the aorta* is attributed to turbulence set up at the stricture itself rather than in col lateral vessels The murmur sounds a little late and may spill through the second sound into early diastole It is heard in the epigastrium or over the lumbar spine when the stricture is in the abdominal aorta

11 *The diastolic murmur of aortic incompetence* (fig 2 32f) is relatively high pitched and best heard with the diaphragm type of chest piece It is situated in the aortic area down the left border of the sternum, and over the left ventricle at the apex beat The murmur begins immediately after the aortic second sound and when loud persists throughout diastole in diminuendo fashion When the leak is very slight, however the murmur may be faint and short and then its greatest intensity is appreciably after the second heart sound indeed when only maximum vibrations

heard the murmur appears to be separated from the second heart sound by a distinct gap This is because the greatest backward flow does not occur until the left ventricular pressure has fallen to zero. A diastolic aortic thrill favours syphilis or a perforated cusp but not exclusively A whining diastolic murmur has a similar meaning

12 *The diastolic murmur of pulmonary incompetence* is similar in quality and timing to the aortic diastolic murmur but is usually confined to the second and third left intercostal spaces It is nearly always functional being due to pulmonary hypertension as described by Graham Steell (1888) or to dilatation of the pulmonary artery without hypertension occasionally it is due to organic disease of the valve as in pulmonary stenosis after bacterial endocarditis or valvotomy It may be accompanied by a thrill

13 *The soft apical diastolic murmur of active mitral valvulitis* was well described by Carey Coombs (1924) It is low pitched relatively short diminuendo and separated from the second heart sound by an appreciable gap representing the time interval between aortic valve closure and rapid ventricular filling (fig 2 32g) The murmur is best heard with the bell stethoscope when the patient lies on the left side and is attributed to turbulence set up by inflammatory thickening of the mitral cusps It is one of the few murmurs practically never accompanied by a thrill

14 *The functional apical diastolic murmur* due to a torrential mitral blood flow is similar to the Carey Coombs murmur in all respects It may be heard in patent ductus ventricular septal defect complete heart block thyrotoxicosis and anæmia The mitral diastolic murmur sometimes associated with coarctation of the aorta and congenital aortic stenosis is not yet fully understood but is probably either rheumatic or due to some degree of fibroelastosis

15 *The apical diastolic murmur of mitral stenosis* is louder and usually rougher than those just described and is commonly preceded by the mitral opening snap (fig 2 32h) The murmur is long and in well developed uncomplicated cases continues to the next first heart sound A thrill is frequently associated In many cases of organic mitral incompetence a rough mitral diastolic murmur is also heard but it is short and follows a loud third heart sound instead of a snap (fig 2 32i)

16 *The diastolic murmur of atrial septal defect* gives rise to the same triple rhythm cadence as mitral diastolic murmurs for it is almost certainly due to a torrential tricuspid blood flow The murmur may be heard best at the apex beat where it may encourage a false diagnosis of Lutembacher s syndrome or near the left sternal edge sometimes as high as the third space, but may be maximum anywhere over the dilated right ventricle It is characteristically accentuated by inspiration which increases the tricuspid blood flow but not that through the atrial septal defect

17 *The continuous machinery murmur of patent ductus* (Gibson 1900) often accompanied by a thrill is more or less localised to the pulmonary area It waxes during systole and early diastole and wanes in late diastole (fig 2 32j) A similar murmur is heard in aorto pulmonary septal defect

18 *Continuous murmurs* waxing and waning in similar fashion are also heard on either or both sides of the chest usually high up anteriorly in cases of pulmonary atresia and are due to broncho pulmonary anastomatic (arterial) communications single or multiple

19 *The jugular venous hum* discussed at length by Potain in 1867, is also continuous and physic in quality Although best heard over the jugular veins themselves it may be first detected when auscultating the aortic or pulmonary area It is loudest in the sitting or standing position is sharply accentuated during inspiration, and usually disappears when the subject lies flat The murmur is also abolished immediately if the jugular blood flow is temporarily halted by digital compression on the vein (usually the right) or by the Valsalva manœuvre

20 Other *continuous machinery murmurs* over the heart may be caused by perforation of an aortic sinus into the pulmonary artery right ventricle or atrium or by coronary arterio venous fistula and over any part of the chest by pulmonary arterio venous fistula

21 *So called functional murmurs* have led to great confusion In a sense all murmurs are an expression of function and in a very strict sense some very important valve murmurs are functional e g certain mitral diastolic murmurs and the Graham Steell murmur If the term is used at all it should mean either murmurs due to turbulence set up by increased blood flow alone the anatomy of the heart at the site of origin of the murmur being normal or murmurs due to functional changes in anatomy In the first group functional murmurs so defined include aortic and pulmonary systolic murmurs associated with hyperkinetic circulatory states the pulmonary systolic murmur of atrial septal defect the mitral diastolic murmur of patent ductus ventricular septal defect etc and the jugular venous hum and in the second group we have the Austin Flint murmur the systolic murmurs of functional mitral or tricuspid incompetence basal systolic murmurs associated with functional dilatation of the aorta or pulmonary artery and the Graham Steell murmur of functional pulmonary incompetence

To dismiss a murmur as functional is unpardonable A functional murmur is not insignificant and is certainly not meaningless nor does it refer exclusively to extracardiac murmurs although at least one of these is functional e g the cardio respiratory murmur This is attributed to systolic decompression of some segment of lung which is compressed by the expanding heart during diastole thus it is a vesicular murmur similar to the sound of inspiration It varies with posture and respiration

EXAMINATION OF OTHER SYSTEMS

Thorough examination of all the other systems of the body should never be neglected in a presumed cardiological case not only as a matter of principle but also because important clues to cardiovascular diagnosis may lie outside that system Partly to emphasise this point a special section has already been devoted to examining the extremities Space forbids dealing with these other systems in a comprehensive manner and since to do so in a niggardly fashion would be valueless no purpose would be served by pursuing the subject further

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CHAPTER III

ELECTROCARDIOGRAPHY

ELECTROCARDIOGRAPHY was discovered in relation to the frog's heart by Kolliker and Muller (1856) and was proved applicable to the study of the heart in man by Waller (1887) who used a capillary electrometer and an antero posterior chest lead It was elaborated by Einthoven (1903) inventor of the string galvanometer and author of the famous triangle which bears his name and used extensively by Lewis (1925) in his well known researches on abnormalities of rhythm In recent years many attempts have been made to place electrocardiography upon a more scientific and less empirical basis and considerable success has been achieved in this respect especially by Wilson and his colleagues (1930 *et seq*) It is not easy (or necessary) for the ordinary physician unless he also be a physicist and mathematician to grasp the electrical details involved but the following simplified account will be readily understood

Certain molecules in the resting cardiac muscle cell dissociate into positive and negative ions The positively charged ions (cations) are distributed on the outer surface the negatively charged ions (anions) within (Curtis and Cole 1941) Such a cell is in a state of electrical balance and is said to be polarised (fig 3 01a) When the cell is excited its polarity is reversed the negative charges coming to the surface the positive charges passing within and the cell is said to be depolarised (fig 3 01b) It should be clear that when a number of cells are clustered together all in the resting polarised state or all in the excited depolarised state there can be no potential differences anywhere on their collective surface If a group of cells were in the process of being excited however those already depolarised would possess negative surface charges whereas those still polarised would have positive surface charges and the collective surfaces of the two sets would yield a potential difference (fig 3 01c) This constitutes a doublet (Craib 1930) dipole (Ashman 1948) or double layer (Bayley 1943) Thus when an excitatory wave flows through cardiac muscle its head is electrically positive and its tail negative (fig 3 01d) If electrodes are placed at A and B and connected to a galvanometer an electrical current flows from B to A through the galvanometer and from A to B through the tissue The excitatory process or accession wave as it is called causes a very rapid or almost instantaneous reversal of cellular polarity so that the duration of the galvanometric deflection is brief and practically indicates the speed of the wave if the muscle thickness is known or the muscle thickness if the speed of the wave is known When the impulse reaches B (fig 3 01e) the whole muscle block AB has a negative collective

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surface if recovery has not yet commenced at A and there is no potential difference between A and B Within a short time however recovery begins at A (fig 3 01f) and the cells become repolarised their collective surfaces becoming positively charged again While the recovery process or regression wave as it is called is spreading from A towards B a current again flows through the galvanometer but in the opposite direction The regression wave travels at the same speed as the accession wave, but causes a slower change of polarity, so that the galvanometric deflection is not so brief If the movements of the galvanometer are graphically recorded the passage of an excitatory impulse from A to B results therefore in a diphasic curve such as that shown in figure 3 02, the first deflection being quick or sharp the second slow or blunt Moreover if the neuro muscular tissue is uniform in all relevant respects the area occupied by the first deflection which may be measured by means of a planimeter with suitable magnification is exactly equal though of opposite sign to the area occupied by the second deflection In modern electrocardiographic parlance the first deflection is represented by the P wave when it reflects atrial excitation and by the QRS complex when it reflects ventricular excitation while the second is represented by the Ta and T waves respectively The QRS complex is written as the accession wave flows through the heart muscle from endocardial to epicardial surfaces not as the excitatory impulse passes down the bundle of His bundle branches and Purkinje network As the heart is not a uniform muscle block but a bi ventricular organ composed of numerous intertwining S shaped muscle bundles (Robb and Robb 1938) the initial ventricular deflection (QRS) is not monophasic as in figure 3 02 but complex and usually biphasic or triphasic nor is the second ventricular deflection (T) of equal area and opposite sign On account of this complexity, it is impossible in the light of present knowledge to determine by scientific theory precisely what an electrocardiogram should look like it is only possible to find out by the practical method For this reason electrocardiography has largely remained an empirical study

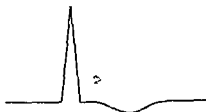


Fig 3 02—The diphasic curve produced by the processes of excitation and recovery in heart muscle

Einthoven s string galvanometer consists of an exceedingly fine fibre such as silver coated glass suspended between the poles of an electro magnet when a current passes through the fibre the latter is deflected towards one or other pole according to the direction of the current By suitable magnification and illumination the movements of the shadow of this string may be recorded on a moving photographic film Valve amplifying oscillographs of various forms operated by potential differences may be used instead of Einthoven s instrument Time marking is so arranged that fine vertical lines appear on the film at inter

0 04–0 05 second, preferably with thicker lines every 0 20 second Horizontal lines for measuring voltage are spaced at intervals of 1 mm

Practical points to bear in mind include satisfactory insulation of the machine and lead wires to prevent 50 cycle A C interference proper standardisation of the galvanometer so that a deflection of 1 cm represents a potential difference of 1 mv and the elimination of skin resistance by means of electrode jelly The paste described by Jenks and Graybiel (1935) has proved effective it consists of sodium chloride 2950 G (6 5 lb) powdered pumice 3600 G (8 lb) gum tragacanth 226 G (8 oz) potassium bitartrate 114 G (4 oz) glycerol 710 ml (24 oz) phenol 28 5 G (1 oz) and water to 7 5 litres (2 gallons) The electrolytes are dissolved in one gallon of water while the gum and glycerol are heated for six hours in the other the two are then mixed stirred and reheated for one hour Phenol and pumice (and more water if necessary) are then added and mixed until the preparation has the consistency of cream Fresh soft green soap (B P) is very little inferior especially after rubbing the skin with some abrasive (Bell Knox and Small 1939) A number of satisfactory pastes or gels are marketed

CHEST LEADS

Analysis of electrocardiograms has become simplified since the introduction of Wilson s neutral electrode (Wilson 1934) Previously all electrocardiograms were bipolar and registered the potential differences between two electrodes placed at different sites on the surface of the body each gathering different potential values According to Einthoven s theory however the algebraic sum of the potentials at the left arm right arm and left leg always equal zero these points representing the apices of an equilateral triangle in the frontal plane of the body the heart lying at its centre and the limbs being regarded as extensions of the lead wires * Thus it is only necessary to link up these three points to a common terminal (preferably through a resistance of 5 000 ohms in order to neutralise differences in skin resistance) to provide an electrode that remains at zero potential throughout the cardiac cycle If this neutral or indifferent electrode is linked to one arm of the galvanometer the instrument will record the potential variations of an exploring electrode linked to the other arm This is the basis of all V leads V standing for potential value or voltage at any particular point It has been agreed that positivity of this exploring electrode should be represented by an upright electrocardiographic deflection

It is now necessary to consider the variations in potential that may be recorded if the exploring electrode is placed over the surface of the left ventricle in man (Wilson *et al* 1944) As the accession wave spreads from endocardial to epicardial surfaces the left ventricular cavity (in contact with the tail of the wave) becomes electrically negative and the surface of the heart (in contact with the head of the wave) becomes electrically positive The galvanometer therefore records an upright or positive deflection R (fig 3 03b) When the accession wave reaches the surface the exploring

* The mathematical proof of this equation is given by Wilson *et al* (1946) Goldberger 1947) and by others

electrode undergoes an abrupt reversal of polarity and the galvanometer registers a sharp downward deflection (the intrinsic deflection) As both the cavity and surface of the left ventricle are then at the same negative potential the electrical field is abolished and the galvanometer comes to rest (fig 3 03c) A complication arises however, because the accession wave starts at some point (such as the left side of the interventricular septum) remote from the muscle underlying the electrode The left ventricular cavity thus becomes negative before the muscle under the electrode

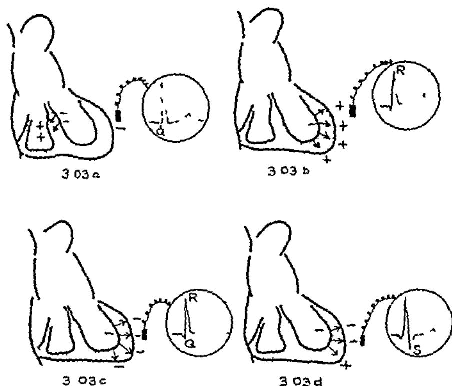


Fig 3 03—Formation of the Q R and S waves (see text)

begins to be actuated and this negative potential is passively transmitted to the surface to be recorded as an initial downward deflection Q (fig 3 03a) Since leads taken from the right ventricular cavity show an initial positive deflection in practically all instances it is believed that the excitation wave starts on the left side of the septum Again if the accession wave is still spreading through muscle remote from the exploring electrode when the galvanometer has registered the local intrinsic deflection the electrical field is maintained and continued negativity of the cavity is passively transmitted to the surface under the electrode to be recorded as a final downward deflection S (fig 3 03d)

When the exploring electrode is placed over the right ventricle similar principles hold good but the right ventricle is much thinner than the left

and therefore the local potential differences are smaller and are normally overpowered by left ventricular events An initial R wave is almost invariable and represents the positive potential produced in the right ventricular cavity as the accession wave spreads through the septum from left to right, in other words it is the head of the left ventricular Q wave Further development of R as excitation passes through the anterior wall of the right ventricle is more or less prevented by the stronger negative potential induced by the tail of the accession wave that is spreading through the left ventricle this is represented by a large S wave Q is never seen over a normal right ventricle The second ventricular deflection T is upright over the left ventricle but may be inverted over the right (in leads V_1 and V_2)

With the aid of unipolar intramural electrodes Prinzmetal and his colleagues (1953) have proved that the inner third of the myocardium is electrically silent as if the Purkinje network penetrated to this depth Subendocardial leads always yield monophasic QS waves and R only begins to develop when the electrode is nearly half way between endo cardial and epicardial surfaces As the electrode approaches the surface R increases rapidly in amplitude while S diminishes

In clinical electrocardiography multiple chest leads are designated leads V_{1-7} The figures indicate the position of the proximal electrode with reference to the chest wall and represent respectively the right and left borders of the sternum the left para sternal and mid clavicular lines and the anterior mid and posterior axillary lines, at the level of a line passing from the fourth intercostal space at points 1 and 2 to the fifth intercostal space at point 4 and thence horizontally (fig 3 04) For routine purposes leads V_1 V_3 and V_5 or V_2 V_4 and V_6 are usually sufficient but in particular instances other combinations or all seven leads are preferable A typical record obtained with this technique is illustrated in fig 3 05 Over the left ventricle (V_5 and V_6) there is a small Q wave a large R wave no S wave an iso potential R T junction and an upright T wave In the transition zone (V_3–V_4) Q has disappeared a conspicuous S wave has developed and T is sharply upright Over the right ventricle (V_1) there is again no Q wave, R is small S large and T is flattened In normal subjects the P wave is upright or occasionally diphasic (3 per cent) in V_2 but often diphasic (20 per cent) or inverted (15 per cent) in V_1 Q is usually present

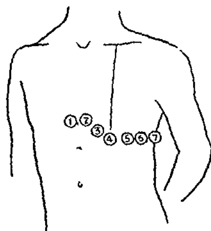


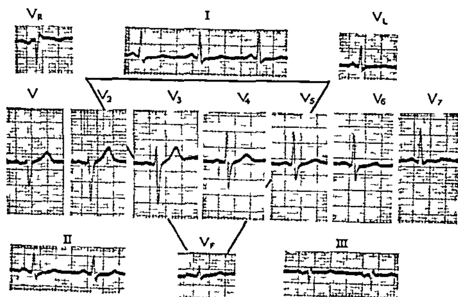
Fig 3 04—Multiple chest leads V_1–V_7 Position of the exploring electrode

V_R I V_L

V_1 V_2 V_3 V_4 V_5 V_6

II V_F III

(a) Average normal



(b) Clockwise rotation about longitudinal axis

Fig 3 05—Normal chest lead electrocardiogram

(c)—Anti clockwise rotation

Fig 3 05—Normal chest lead electrocardiogram (V –V)

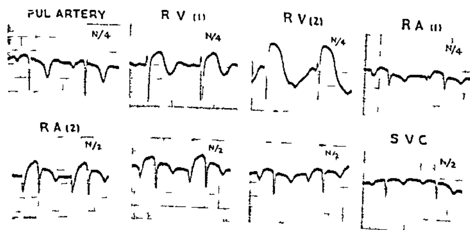


Fig 3 06—Right ventricular and pulmonary artery cavity leads

in V_6 occurs in V_5 in 45 per cent of cases but is rarely seen farther to the right S is usually absent in V_{6-7} *is absent in* V_5 *in 17 per cent of cases,* but is invariably found in V_3 and V_1 T is always upright in V_4–V_6 may be occasionally diphasic in V_3 and is inverted in V_1 in 62 per cent of cases

If there is clockwise rotation about the longitudinal axis (viewed from below) the anterior surface of the septum is shifted to the patient s left this means that S is dominant in V_4 the transition zone being shifted to V_4 or V_5 In such cases Q may not appear until V_6 or V_7 Similar graphs are obtained when the heart is horizontal in position the septum then being displaced to the patient s left (fig 3 05b)

Anticlockwise rotation about the longitudinal axis brings the anterior surface of the septum to the patient s right The QR pattern may then be seen from V_6 to V_3 and the transition zone is shifted to V (fig 3 05c)

In addition to leads V_1–V other positions of the exploring electrode *have been used with advantage under exceptional circumstances An œsophageal lead may also be helpful in doubtful cases of posterior myo* cardial infarction and an intracardiac lead may provide interesting information but these are rarely necessary for clinical purposes

The œsophageal lead takes its potential from the surface of the left atrium when high and from the posterior surface of the left ventricle when low Left atrial potentials are transmitted from the cavity of the left ventricle and show monophasic Q waves and inverted T waves the cavity of the left ventricle being negative throughout the inscription of the initial and second ventricular deflections The posterior surface of the left ventricle gives rise to a QR complex similar to that obtained anteriorly or laterally Œsophageal patterns therefore show monophasic Q waves or QR deflec tions Q dominating when the electrode is relatively high up R when the electrode is relatively low down T is usually negative when the electrode is high positive when low

Intracardiac leads from the cavity of the right ventricle show a small initial R wave followed by a deep S wave as already described If the catheter is passed through a patent foramen ovale into the left ventricle a monophasic Q wave is obtained When the catheter is passed into the pulmonary artery the small R wave seen within the cavity of the right ventricle disappears in favour of a monophasic Q wave (fig 3 06) this is because the pulmonary artery takes its potentials from the surface of the left auricle

There are thus only a limited number of basic QRS patterns upon which all ventricular deflections encountered in clinical electrocardiography de pend (fig 3 07) the QR complex of a left ventricular surface lead (T normally upright) the RS complex of a right ventricular surface lead (T usually upright) the monophasic Q wave of a left ventricular cavity lead (T normally inverted) the RS complex of a right ventricular cavity lead (T normally inverted) and the balanced QR pattern of a combined left

ventricular cavity and surface lead from the back of the heart (Goldberger 1947)

The direction of the second ventricular deflection T is opposite to theoretical prediction in all the basic patterns and suggests that the

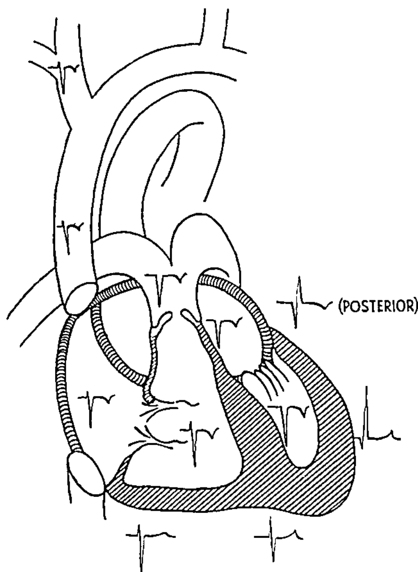


Fig 3 07—The basic QRS T patterns

recovery wave starts at the surface of the ventricles and is directed towards the cavities

Instead of V leads many workers including Wolferth and Wood (1932–33) who re introduced chest leads to clinical electrocardiography have coupled the exploring electrode with a relatively indifferent electrode

placed on the right arm (CR) or on the left leg (CF) Agreement will never be reached as to which of these is the more informative and it is expected that they will both be abandoned in favour of V leads They will be considered in greater detail in subsequent paragraphs

UNIPOLAR LIMB LEADS

The potential values in the right arm (V_R) left arm (V_L) and left leg (V_F) may be obtained by placing the exploring electrode on the desired limb *and linking it with Wilson's neutral electrode* As unipolar limb leads are of low voltage it is customary to alter the standardisation so that a potential difference of 1 millivolt causes a deflection of 15 mm (instead of 10 mm) Alternatively Goldberger's augmented leads may be used With *this technique the V lead is attached to the limb the potential values of* which are being measured whilst the wire connecting this limb with the central neutral terminal is detached and left hanging free The potentials are thus increased by 50 per cent (Goldberger 1942) thus

$$\text{Since } V_R + V_L + V_F = O$$
$$\text{then } V_L + V_F = -V_R$$

Now when an electrode on the right arm is paired with a central terminal linked to the left arm and left leg the galvanometer records $V_R - \dfrac{V_L + V_F}{2}$ the latter being the mean potentials of the left arm and left leg

$$\text{Now} \quad V_R - \frac{V_L + V_F}{2}$$
$$= V_R - \frac{(-V_R)}{(\ 2\ )}$$
$$= V_R + {}^1V_R = 1{}^1V_R$$

There has been some confusion concerning the equation $V_L + V_R + V_F$ = zero This statement is obvious in relation to the technique used for obtaining the unipolar limb lead potentials for the neutral electrode (e) employed with this technique is the mean of the potential values in each of the three limbs i e $e = \dfrac{L+R+F}{3}$

$$\text{Now } V_L = L - e$$
$$V_R = R - e$$
$$V_F = F - e$$
$$\text{So that } V_L + V_R + V_F = L + R + F - 3e$$
$$= L + R + F - \frac{3(L+R+F)}{3}$$
$$= \text{zero}$$

It should be readily appreciated that this self evident fact has no bearing on whether the common terminal is neutral or otherwise but would be true for any value of e Thus the statement does not imply the truth of

Einthoven's hypothesis nor the validity of the theory underlying Wilson's neutral electrode

Unipolar limb leads are useful in determining the electrical position of the heart in explaining the difference between CR CF and V chest leads and in demonstrating the basis of the standard leads V_R usually shows inversion of all complexes because it reflects the negative potential of the cardiac cavities transmitted through the great vessels (figs 3 07 and 3 08)

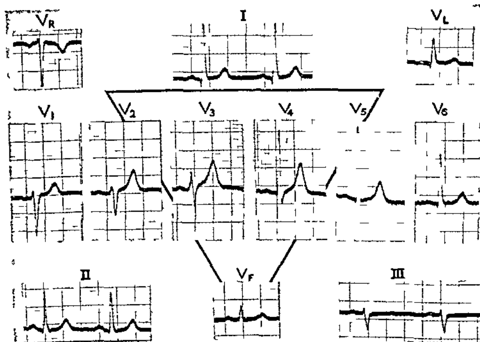


Fig 3 08— Unipolar limb leads (V_L V_R V_F) and standard leads 1 2 and 3
(a) Normal (the heart is more horizontal than vertical)

When the heart is normal in size and position V_L and V_F are mainly positive dominant left ventricular surface potentials being transmitted more or less equally to both of them (fig 3 08a) When the heart is electrically horizontal however left ventricular surface potentials are transmitted more strongly to the left arm and right ventricular surface potentials to the left leg There is then a small Q and tall R wave in lead V_L and a small R and deep S wave in lead V_F (fig 3 08b) When the heart is electrically vertical the negative potentials of the cavities are transmitted more strongly to the left arm and the left ventricular surface potentials more strongly to the left leg There is then a small R and deep S wave in V_L and a small Q and tall R wave in V_F (fig 3 08c) In normal subjects the electrical position of the heart is more or less in line with its anatomical position

Fig 3 08 (b)—Horizontal heart

Fig 3 08 (c)—Vertical heart

The differences between CR, CF and V chest leads may now be appreciated CR leads are V leads minus the potentials in V_R whilst CF leads are V leads minus the potentials in V_F As V_R potentials are negative their subtraction from V in CR records makes all deflections more positive – not only is R taller in lead CR_1 but T is invariably upright in adults and in children over eight years of age Again since V_F potentials are normally positive their subtraction from V in CF records makes all deflections more negative As the voltage is usually higher in V_R than in V_F however, CR leads show greater differences from V leads than do CF leads

STANDARD LEADS

Einthoven s bipolar leads introduced at the beginning of the century and adopted as the standard leads throughout the world consist of the left and right arm (lead I) the left leg and the right arm (lead II) and the left leg and left arm (lead III) Electrocardiograms derived from these leads can be calculated of course from the deflections obtained with unipolar limb leads for lead 1 equals V_L–V_R lead II equals V_F–V_R lead III equals V_F–V_L The subtraction of the negative potentials in V_R from the positive potentials in V_L and V_F result in strongly positive QRS and T deflections in leads I and II Again as the voltage of R in V_F is usually higher than that in V_L QRS is also normally positive in lead III

By definition there is an obvious relationship between the three standard leads

$$\text{lead II} = \text{lead I} + \text{lead III}$$

This merely states that

$$V_F - V_R \text{ (lead II)} = V_L - V_R \text{ (lead I)} + V_F - V_L \text{ (lead III)} = V_F - V_R$$

and has nothing to do with Einthoven s theory or triangle

The relationship between the standard leads and the Wilson unipolar limb leads is as follows

$$V_L = \frac{\text{I}-\text{III}}{3}$$

$$V_R = \text{minus } \frac{\text{I}+\text{II}}{3}$$

$$V_F = \frac{\text{II}+\text{III}}{3}$$

The augmented values obtained with Goldberger s technique may be derived from the standard leads by changing the denominator in the above equations from 3 to 2

NORMAL APPEARANCES

(Fig 3 08)

P wave

P represents the excitation process as it spreads from the sinoauricular node through both atria It is usually blunt and is upright in leads I and

II but may be inverted in lead III Its height should not exceed 2 0 mm and its duration 0 1 second Following P slight depression of the base line sometimes hidden by the QRS complex may be evident and represents atrial recovery or repolarisation It has been termed the atrial T wave or Ta wave

P–R interval

No deflection is caused by the passage of the excitatory impulse down the bundle of His its main branches and Purkinje network so that there is an iso potential interval between atrial and ventricular events this is the P–R interval and is conveniently measured from the beginning of P to the beginning of QRS It commonly ranges between 0 12 and 0 20 second but occasionally even in young subjects it may measure 0 21 or 0 22 second without evidence of heart disease or of general ill health

The P–R interval is little affected by spontaneous variations in heart rate but may be slightly reduced by atropine and slightly lengthened by carotid sinus compression Vagal tone has a much greater effect on the sinus node than on A–V conduction

The QRS complex

Q R and S when all are present form a triphasic complex representing the spread of the accession wave through the ventricles and are convenient symbols for describing the shape of the initial ventricular deflection Each is applied to a wave so defined by its direction and by its time relationship to the others Thus any upward deflection is called R or if there are two such R and R A downward deflection is called Q if it precedes R or if it is the only wave present and S if it follows R

Q rarely measures more than 1 or 2 mm in leads I and II and is often absent altogether in lead III, however, it may be conspicuous and may measure up to one third of the amplitude of R R should exceed 5 mm in height in the most favourable lead unless the spatial vector is unusually postero anterior Slight notching or slurring near its base is common and has no significance Distortion of the apex of R is rare in normal subjects but may be disregarded when unaccompanied by other changes S is variable, and is greatly influenced by axis deviation which will be considered later

The whole QRS complex should not exceed 0 1 second in duration and rarely exceeds 0 08 second in normal individuals

RS–T segment

This refers to that short segment between the QRS complex and the T wave i e between the end of the excitatory and the beginning of the recovery processes In some cases this is so short as to represent merely the RS–T junction Any deviation of the RS–T segment from the iso potential

base line should be regarded with suspicion Slight deviation of the order of 0 5 mm. may be within normal limits yet taken in conjunction with other findings may be highly significant

It is customary to include the proximal portion of the T wave when describing the shape of the RS–T segment e g whether concave, straight or convex Speaking in this way a normal RS–T segment curves gently from its point of origin in the direction of the T wave it is neither straight, nor does it deviate in the opposite direction first

T wave

T represents the recovery process or the regression wave (repolarisation) and is known as the second ventricular deflection It is normally upright in leads I and II but may be inverted in lead III It should measure at least 2 mm in amplitude in the most favourable lead

Q–T interval

The interval between the beginning of QRS and the end of T represents the total time occupied by ventricular excitation and recovery It is inversely proportional to the heart rate ranging between 0 42 second at a speed of 48 per minute and 0 28 second at a speed of 110 The formula of Bazett (1920) is $Q–T = K\sqrt{C}$ where C represents the cycle length The constant K is variously given as 0 38—0 39 plus or minus 0 04 and is a trifle longer in women than in men and children

Taran and Szilagyi (1947) have made the sensible suggestion that the Q–T interval should be recorded as corrected for rate i e as $Q–T_c$ This should equal Bazett s constant K i e the actual Q–T interval when the heart rate is 60 per minute or when the cycle length is one second $Q–T_c$ is easily calculated with the aid of a slide rule when the actual Q–T interval and cycle length are known for Q–T (or $K) = \frac{Q–T}{\sqrt{C}}$ The Q–T interval is lengthened by hypocalcæmia (fig 3 33) and shortened by digitalis (fig 3 27b) $Q–T_c$ may be prolonged in active rheumatic carditis (Taran and Szilegyi 1947) There is some evidence that Q–T is also lengthened by cardiac enlargement from any cause and shortened by cardiac compression as in pericardial effusion (Van Lingen 1947)

U wave

Following T and coinciding with the super normal recovery phase a small rounded positive deflection the U wave may be seen Its significance is not fully understood but it appears to be exaggerated in chest leads taken from the right of the interventricular septum and to be flattened or even inverted in leads taken from the left of the septum when there is left ventricular hypertrophy and vice versa when there is right ventricular hypertrophy It may also be inverted in left ventricular surface leads during an attack of angina pectoris It is accentuated by digitalis

THE CARDIAC VECTOR

Maximum potential differences within the heart at any given moment may be represented in magnitude and direction by a line of appropriate length and spatial direction (drawn from the hypothetical centre of electrical events) which may be called a vector and its direction a spatial axis Both magnitude and direction of this vector alter from moment to moment during the phases of ventricular excitation and recovery but may be resolved into mean values If such a vector is projected on to the frontal plane of the body its new momentary or mean manifest value may be calculated by suitable measurements, detailed below of the electrocardiograms obtained from any two of Einthoven s leads for the frontal plane or manifest vector may be projected on to the sides of an equilateral triangle the apices of which are represented by the left and right arms (or shoulders) and by the left leg (or symphysis pubis) the sides of the triangle thus representing the three standard leads For example if the line AB (fig 3 09) represents the maximum momentary manifest QRS vector i e if it

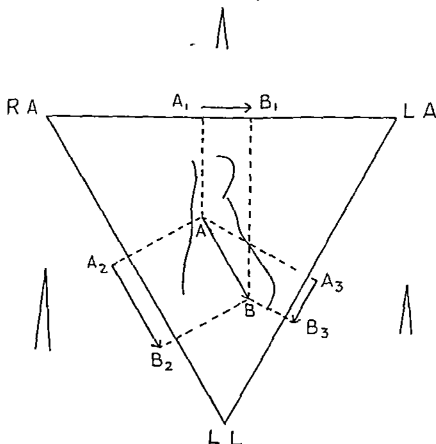


Fig 3 09—Projection of the frontal plane QRS vector on to the sides of Einthoven s equilateral triangle

represents the projection on to the frontal plane of the body of a line in space representing the magnitude and direction of maximum potential differences generated within the heart during the period of ventricular excitation then the lines A1–B1 A2–B2 and A3–B3 obtained by projecting the line AB on to the sides of Einthoven s equilateral triangle give the magnitude and direction of the maximum QRS deflection in leads I II and III respectively Moreover it can be easily shown that at any given moment the amplitude of the QRS deflection in lead II equals the algebraic sum of that in leads I and III or the amplitude of the QRS deflection in any one lead equals the algebraic sum of that in the other two The same law applies to atrial activity and to the recovery phase i e to the P Ta and T waves and to mean as well as momentary values Conversely if the magnitude and direction of the QRS complex at any given moment is known in any two leads their resultant drawn from the centre of Einthoven s triangle represents the manifest (frontal plane) vector of QRS at that particular moment and its direction the manifest electrical axis In current electrocardiographic nomenclature the electrical axis refers to this resultant frontal plane axis as obtained from the maximum upright QRS deflection in any two leads if apparently synchronous and is expressed in terms of its angle with the horizontal being plus when rotated clockwise from this base minus when anti clockwise As so expressed the normal electrical axis lies between 0 and 90 degrees and has a wider range than the frontal plane anatomical axis

Triaxial reference system

For convenience Einthoven s triangle may be suitably represented as a triaxial reference system (Bayley 1943) The lines representing the three sides of the triangle are transposed so that they intersect at a common point O (fig 3 10) The horizontal line RL then represents lead I and the

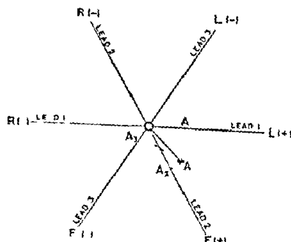


Fig 3 10—Bayley s triaxial reference system

lines RF and LF leads II and III respectively The customary signs are preserved so that R is negative L positive and L negative or positive as shown in the diagram If the vector OA, is projected on to these lines its value in the standard leads may at once be determined by the lengths OA1, OA2 and OA3 The converse may be applied with equal simplicity

By measuring the net area of QRS in any two leads (instead of momentary synchronous points) by means of a planimeter and suitable magnification (or by dividing the amplitude of the wave by half its width) the area below the base line being subtracted from that above the resultant mean axis of QRS in the frontal plane can be determined in similar fashion (Wilson *et al*, 1934) Measurements may be made in millivolt seconds microvolt seconds or in suitable units based on voltage × time (Ashman and Byer 1943) Such a resultant drawn from the centre of Einthoven s triangle having both magnitude and direction, is called the mean QRS vector in the frontal plane or the manifest mean QRS vector and its direction the manifest mean QRS axis Manifest mean vectors for T and P may be similarly obtained Bayley (1943) has suggested that the symbol Â might well designate the axis of such vectors and the symbol A their magnitude the manifest mean axis of QRS would then be called ÂQRS and its magnitude AQRS

If the heart were a simple uniform muscle block the algebraic net area occupied by QRS and T would be zero as it is not the net area of QRST has a positive or negative value which if measured in any two leads may be resolved into a vector drawn from the centre of Einthoven s triangle The axis of this vector or the manifest mean QRST axis (ÂQRST) has been called the ventricular gradient (Wilson Macleod and Barker 1931) or Ĝ and its magnitude G The gradient represents the magnitude and direction of maximum local variations in the speed of the processes of excitation and recovery whereby the heart differs from a uniform muscle-block

The manifest mean axis of QRS averages about 60 degrees that of T about 50 degrees The ventricular gradient in hearts which are not anatomically rotated ranges between 45 and 65 degrees On the whole hearts which are relatively central in position i e rotated clockwise (viewed from the front) about their antero posterior anatomical axis are also rotated clockwise (viewed from the apex) about their longitudinal anatomical axis and show clockwise deviation i e deviation to the right of all manifest momentary and mean electrical axes, but the greatest shift occurs with the ordinary momentary electrical axis of QRS and the least with the ventricular gradient This also applies to transverse hearts with anti clockwise rotation and deviation of all electrical axes to the left (Ashman and Byer 1943)

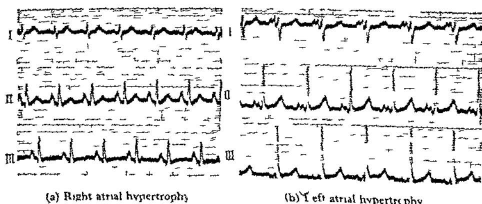
From what has been said it should be clear that the QRS and T vectors in the frontal plane of the body alter in magnitude and direction from moment to moment during the phase of ventricular excitation and recovery As one end of such a vector is fixed at the centre of Einthoven s triangle it follows that the other end must describe a continuous curve Mann (1920)

showed how such curves could be reconstructed and later devised a method of recording them directly (1931) More recently Wilson and Johnston (1938) employing the cathode ray oscillograph published typical curves and called them vectorcardiograms Even these however are restricted to the behaviour of the vector in the frontal plane of the body being so limited by use of the standard limb leads Wire models of spatial vectorcardiograms have been constructed by Duchosal (1949)

ELECTROCARDIOGRAPHIC ABNORMALITIES

ABNORMALITIES OF THE P WAVE

There are four main varieties of P wave deformity the tall sharp P wave of right atrial hypertrophy (fig 3 11a) the conspicuous widened P wave of left atrial hypertrophy which may be bifid rounded or flat topped (fig



(a) Right atrial hypertrophy (b) Left atrial hypertrophy

Fig 3 11—Abnormal P waves

3 11b) the low voltage widened P wave which may be also bifid rounded, or flat topped (fig 3 11c) and the inverted P wave (fig 3 11d)

Tall sharp P waves are characteristic of pulmonary hypertension pulmonary stenosis and tricuspid stenosis The voltage ranges between 2 and 5 mm and as the wave is not widened it becomes peculiarly sharp like an arrowhead They are usually most evident in leads II and III

Conspicuous widened P waves measuring 0 12 second in duration are almost diagnostic of mitral stenosis The voltage may be normal or slightly increased but rarely exceeds 2 5 mm Most examples are bifid the first peak representing right atrial activity the second left atrial activity so that the P mitrale implies delay in left atrial activation (Reynold 1953) They are usually seen best in leads I II and V

P waves similar in shape and width but usually of lower voltage may be seen sometimes in advanced cases of hypertensive heart disease or aortic valve disease It is uncertain whether they represent left atrial

dilatation due to left ventricular failure as originally suggested by Wood and Selzer (1939) or inter atrial block (Berconsky and Kloztman 1945)

Inverted P waves are found in lead I in cases of dextrocardia in leads II and III in coronary sinus rhythm and in all leads in many cases of nodal rhythm



Fig 3 11 (c)—P waves in hypertensive heart failure

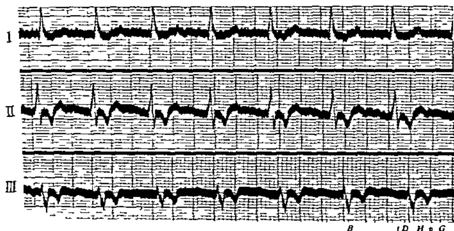


Fig 3 11 (d)—Inverted P waves in nodal rhythm

ABNORMALITIES OF THE QRS COMPLEX

Axis deviation

It has already been pointed out that the electrical axis of the heart refers to the frontal plane projection of the maximum momentary spatial vector and usually lies between 0 and 90 degrees more or less in the anatomical axis Anti clockwise rotation of the heart about its antero posterior axis (viewed from the front) or about its longitudinal axis (viewed from the

cardiac apex) causes deviation of the electrical axis to the left, so that the frontal plane vector may make a minus angle with the horizontal whilst clockwise rotation about similar axes causes right axis deviation the vector now making an angle of more than 90 degrees with the horizontal Left or right axis deviation respectively also occurs when the left or right ventricle is disproportionately enlarged Moreover left ventricular enlargement is often associated with anti clockwise rotation about both anatomical axes and right ventricular enlargement with clockwise rotation

Reference to Einthoven s triangle will show that if the electrical axis deviates to the left and approaches or surpasses the horizontal lead I becomes the axial lead (fig 3 12) R_I then carries the maximum voltage R_{II} is smaller and the maximum QRS deflection in lead III is downwards, i e the main deflection is S In such cases S_{III} is really the electrical counterpart of R_I Unipolar limb leads commonly show an electrically horizontal heart R in V_L and S in V_R being unusually conspicuous

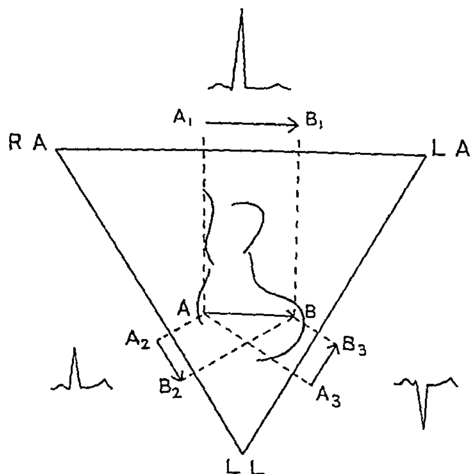


Fig 3 12—Left axis deviation (Einthoven s triangle)

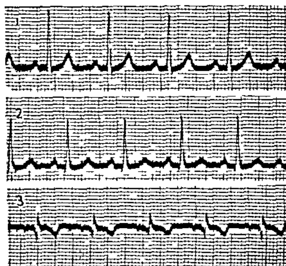


Fig 3 13—Axis deviation due to elevation of the diaphragm (Q_3 S_1 type)

Left axis deviation occurs in 10 per cent of normal individuals, in any condition in which the left ventricle is disproportionately enlarged in cardiac displacement to the left from scoliosis or from intrathoracic causes and when the diaphragm is elevated causing the heart to lie more transversely It may not be possible from examination of the limb lead QRS complexes alone to decide whether axis deviation is due to displacement or to left ventricular preponderance but this distinction may often be made by considering the behaviour of the RS-T segment and T wave and especially by noting the QRS pattern in multiple chest leads (*vide infra*)

A particular form of axis deviation is seen with elevation of the diaphragm as from obesity pregnancy flatulence or ascites R_I is taller than R_{II}, S_I and Q_{III} are prominent and T_{III} is inverted (fig 3 13) In such cases there is no Q wave in lead V_F and the T wave usually remains inverted in lead V_1

When the electrical axis is deviated to the right so that it occupies a more or less vertical position lead III becomes the axial lead (fig 3 14) R_{III} then carries the maximum voltage R_{II} is smaller whilst the maximum deflection in lead I is S which is the electrical counterpart of R_{III} In unipolar limb leads S is conspicuous in V_L and R in V_F Right axis deviation is the rule in newly born infants is common in very young children occurs in 1 per cent of normal children over the age of eight,

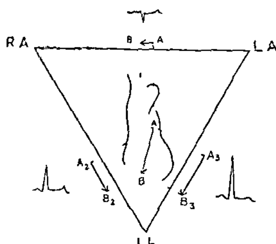


Fig 3 14—Right axis deviation (Einthoven s triangle)

and is rarely seen in strictly normal adults. It may be caused by appropriate cardiac displacement or rotation, and by right ventricular dominance. As with left axis deviation it may not be possible from inspection of the limb lead QRS complexes alone to determine whether the axis shift is due to right ventricular dominance or otherwise but the behaviour of QRS in multiple chest leads may clarify the issue (*vide infra*)

Left ventricular preponderance

When the left ventricle is enlarged the accession wave takes longer to penetrate that chamber and creates more powerful potential differences. Thus R in leads V_5 and V_6 and S in leads V_1 and V_2 have a larger amplitude (R in $V_{4, 5, 6, 8} > 25$ mm S in $V_1 > 15$ mm) the intrinsic deflection in left ventricular surface leads is delayed (longer than 0.05 second) and the width of QRS slightly increased (0.1 second). Secondary changes in the T wave occur in advanced cases the R T segment being depressed

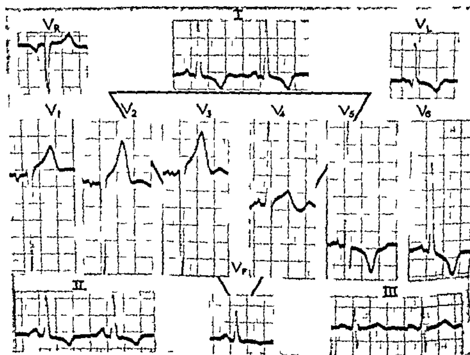


FIG 3 15—Left ventricular preponderance

and T inverted in leads V_5 and V_6 and the S T segment being elevated and T sharply upright in leads V_1 and V_2 (fig 3 15)

When the heart is horizontal which is usual V_L resembles V_5 and V_F resembles V_1 both in respect of QRS and T. The appearances in standard lead I therefore also resemble V_5 or V_6 and those in lead III resemble V_1

When the heart is more or less vertical which is less common left ventricular surface potentials are transmitted more to the left leg There is then no axis deviation in standard leads (Wilson 1944) but high voltage and perhaps T wave inversion in all (fig 3 16) Concordant left ventricular preponderance as it is called is best seen in concentric left ventricular hypertrophy such as may occur in aortic stenosis and malignant hypertension

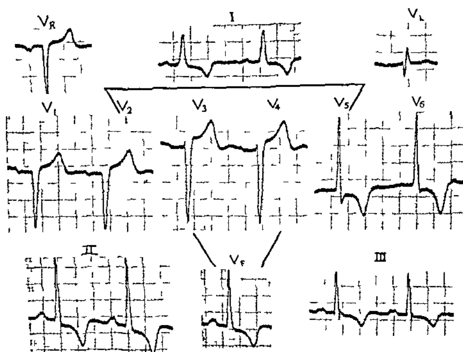


Fig 3 16—Left ventricular preponderance (heart semi vertical)

Right ventricular dominance

When there is gross enlargement of the right ventricle the potential differences generated by the wall of that chamber may approach or even surpass those from the left ventricle Right ventricular surface leads may then truly represent the outward spread of the accession wave beneath the exploring electrode After a small initial septal R wave a tall secondary R replaces the usual S wave in leads V_1 and V and S is conspicuous in V_5 and V_6 (fig 3 17) Secondary inversion of the T wave with slight depression of the R T segment is common in V_1 to V_3 In lesser degrees of right ventricular hypertrophy clockwise rotation about the longitudinal axis (viewed from below) is usually held responsible for the changes Thus the occasional appearance of Q in lead V_1 followed by a tall R wave may be derived from potentials at the back of the heart

As a rule the heart is also vertical in position V_L is strongly influenced by negative cavity potentials and V_F by left or right ventricular surface potentials In other words QRS is mainly negative in V_L and strongly positive in V_F Standard leads therefore show right axis deviation and

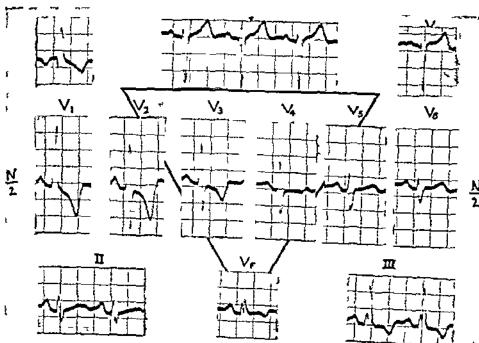


Fig 3 17—Right ventricular dominance (case of pulmonary stenosis)

there may be inversion of the T wave with depression of the R T segment in lead III or in leads II and III When R is dominant in V_1 and S in V_5 right axis deviation also occurs when the heart is horizontal for V_L then reflects V_5 and V_F reflects V_1

Widening of the QRS complex

The accepted maximum normal limit of 0 1 second for the duration of the QRS complex is generous and includes many instances of abnormal widening due to increased thickness of the ventricular walls As the accession wave causes almost instantaneous reversal of polarity in the tissue it excites the width of QRS depends almost entirely on the thickness of the ventricular walls provided the conducting system is normal and assuming that the speed of the wave is constant With extremely hypertrophied hearts it is theoretically possible for QRS to measure as much as 0 12 second in duration but in fact it rarely exceeds 0 1 second It is probably wise to regard anything over 0 11 second as intraventricular block It is found too that widening due to ventricular hypertrophy is usually associated with high voltage whereas in bundle branch block QRS is commonly

notched splintered or heavily slurred When the heart is grossly dilated there may be some delay in the passage of the excitatory impulse down the Purkinje network, causing intraventricular block Some such mechanism may account for the transient right bundle branch block that occurs occasionally in massive pulmonary embolism and for the right bundle branch block so commonly seen with atrial septal defect A Q wave can nearly always be demonstrated in suitable left ventricular surface leads when widening of the initial ventricular deflection is due to left ventricular hypertrophy whereas it is ordinarily absent in left bundle branch block

Widening of the QRS complex is also seen in uræmia when it is due to a raised blood potassium (figs 3 33 and 3 34)

Bundle branch block

In *left bundle branch block* the excitatory process spreads through the right ventricle in normal fashion but does not at first reach the left ventricle As the interventricular septum is excited from the right side the accession wave spreads through it from right to left The cavity of the left ventricle therefore becomes initially positive and this potential is transmitted passively to the surface as an R wave in V_5 or V_6 There can be no Q wave in such leads with a healthy septum When the accession wave reaches the left side of the septum there is an immediate reversal of polarity the left ventricular cavity becoming momentarily negative This negativity is again transmitted passively to the surface V_5 showing a momentary downward deflection following the initial R wave Almost immediately however, the excitatory process spreads throughout the endocardium of the left ventricle and the accession wave begins to flow outwards in the usual way The surface of the left ventricle then becomes actively positive and the true R wave is written When the surface is activated the final intrinsic downward deflection occurs V_5 or V_6 thus exhibits a large widened R wave interrupted by a relatively early notch representing the arrival of the accession wave at the left side of the septum (fig 3 18) Right ventricular surface potentials are influenced at first by a normal right ventricular accession wave and later by the delayed negativity of the cavity of the left ventricle which is passively transmitted through the depolarised septum and right ventricle Thus V_1–V_3 exhibit small R waves early intrinsic deflections and deep wide S waves The total duration of QRS commonly measures 0 12 to 0 16 second As the heart is usually horizontal the V_5–V_6 pattern is seen also in V_L and lead I and the V_1 pattern in V_F and lead III Should the heart be vertical however the V_5–V_6 pattern is transmitted to the left leg and the appearances in standard leads may be mistaken for right bundle branch block (fig 3 18b) Whatever the position of the heart in left bundle branch block deviation of the RS T segment and the direction of the T wave are usually of opposite sign to the main QRS deflection Thus with horizontal hearts the RS T segment is depressed and the T wave inverted in V_5–V_6 V_L and standard lead I

Fig 3 18 (a)—Left bundle branch block (heart horizontal)

Fig 3 18 (b)—Left bundle branch block (heart vertical)

Left bundle branch block may occur in diseases chiefly affecting the left ventricle such as hypertensive heart disease aortic stenosis syphilitic aortic incompetence and ischæmic heart disease in non rheumatic myo carditis cardiac fibrosis and generalised cardiopathy of almost any type and occasionally in otherwise clinically normal hearts although far less commonly than right bundle branch block

In *right bundle branch block* the septum is activated entirely from the left side The potential of the right ventricular cavity is therefore initially posi tive and is passively transmitted to the surface where it may be recorded as the first part of R When the accession wave reaches the right side of the septum the polarity is abruptly reversed and a pseudo intrinsic deflection is recorded at the surface Almost at once however the right ventricular wall is invaded and the surface then becomes actively positive This results in a second R wave and finally in the true intrinsic deflection Leads V_1 and V therefore show a widened notched R wave or a large M complex T is in the opposite direction (fig 3 19a) Over the left ventricle in leads

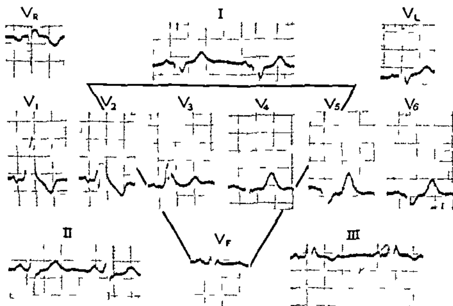


Fig. 3 19 (a)—Right bundle branch block (heart horizontal)

V_5 and V_6 a normal QR wave and intrinsic deflection are followed by a grossly slurred S wave representing delayed negativity of the right ventri cular cavity passively transmitted through the depolarised septum and left ventricle As a rule V_5 and V_6 potentials are transmitted to V_L and form the pattern of standard lead I the M complex of V_1–V is usually seen in V_F and in standard lead III When the heart is vertical however V_1

potentials may be transmitted to V_L and standard leads may look like left bundle branch block (fig 3 19b) Multiple chest leads may be necessary not only to determine which bundle branch is blocked but also to detect the lesion at all in some cases partial right bundle branch block for instance is frequently overlooked in standard leads Right bundle branch

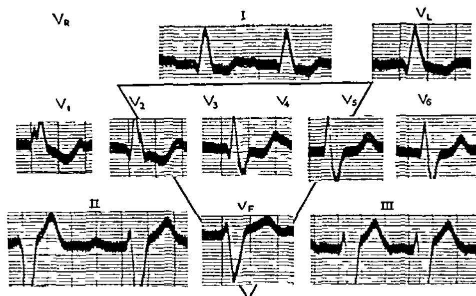


Fig 3 19 (b)—Right bundle branch block (heart vertical)

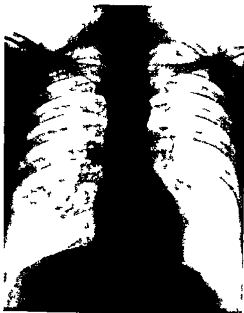
block may occur in any of the diseases that may result in great dilatation of the right ventricle particularly atrial septal defect and Ebstein s disease in ischaemic heart disease and any of the generalised cardiopathies such as isolated myocarditis and by no means rarely in otherwise normal hearts

ABNORMALITIES OF THE RS T SEGMENT AND T WAVE

It is profitable to consider the RS T segment and T wave together and in many cases to consider them also in relationship to the QRS complex for they are all ventricular events The various patterns made up by these three variables in limb and multiple chest leads provide a wealth of information concerning the state of the ventricles in health and disease Secondary inversion of the T wave in relation to QRS changes has already been described

Myocardial infarction

It is customary to describe two types of electrocardiogram associated with myocardial infarction T_I and T_{III} types (Parkinson and Bedford 1927) the first denoting anterior, the second posterior lesions (Barnes and



(a) Postero anterior view



(b) 1st oblique position (right anterior)



(c) 2nd oblique position (left anterior)

Fig 4 03—Teleradiogram of a normal subject

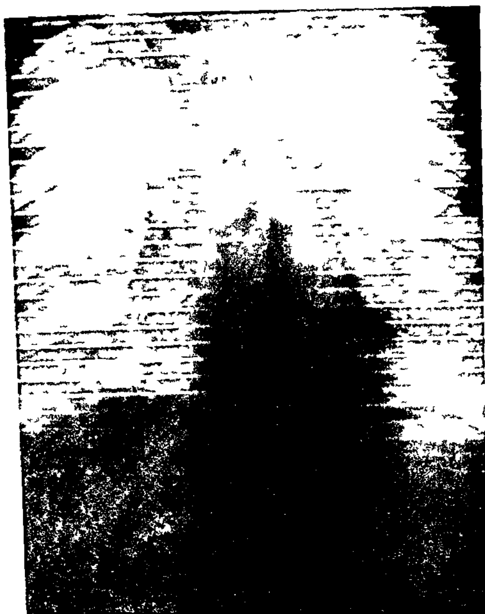


Fig 4 04—Normal kymogram (P A view)
(By urtesy f Dr J er H k)

Whitten, 1929) There is no essential difference in the shape of these two patterns, the difference depending upon the leads in which they are found

If an infarct involves the whole thickness of the muscle wall no accession wave can flow through it The negative cavity potential produced by outward spread of the accession wave through remote healthy muscle is then passively transmitted through the infarct to the surface overlying it An electrode placed over the infarct therefore registers a monophasic Q wave

If the infarct involves only the inner third of the myocardium no electrocardiographic changes occur for this zone is electrically silent (Prinzmetal *et al* 1953)

If the outer layers are patchily involved QR complexes occur at the epicardial surface the initial Q wave is due to transmission of the negative cavity potential and the subsequent R wave to spread of the accession wave through patches of live muscle in the outer layers (Prinzmetal *et al* 1954) R waves of this kind are usually of reduced voltage In anterior left ventricular infarcts these QRS changes may be registered in leads V_3 V_4 V_5 and V_6 being more marked in V_3–V_4 in antero septal infarcts and in V_5–V_6 in antero lateral infarcts They are commonly transmitted to V_L and are therefore seen well in standard lead I (fig 3 20) Similar QRS changes occur in posterior infarcts but are transmitted to V_F and thus to standard lead III (fig 3 21) When the heart is vertical however, typical changes in V_5 from an anterior infarct may be transmitted to lead V_F and hence to standard leads II and III (fig 3 22)

According to Wilson *et al* (1933) partly necrosed muscle sets up a steady current due to the development of potential differences between

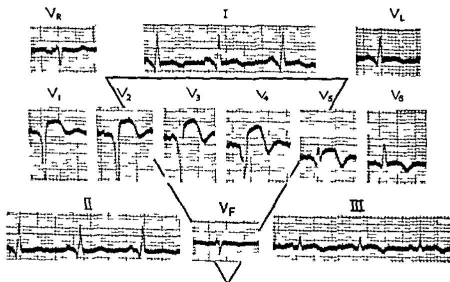


Fig 3 20—Anterior myocardial infarction showing pathological Q waves and elevation of the RS T segment in leads V_{1-4} V_L and standard lead I

Fig. 3.21—Posterior myocardial infarction showing pathological Q waves and elevation of the RS T segment in lead V_F and standard leads II and III

Fig. 3.22—Anterior infarction with vertical heart. Standard leads show changes that simulate those of posterior infarction

(a) Anterior

(b) Posterior

Fig 3.23—Later stages of anterior (a) and posterior (b) infarction showing typical Q waves and inversion of the T wave in appropriate leads

injured and healthy tissue Injured tissue is electro negative, healthy tissue is positive and completely necrosed tissue electrically inert When the injured area involves the outer portion of the ventricular wall the surface is therefore negative the current flowing from without inwards An electrode placed over the infarct registers this negativity by depressing the base line This is shown in the electrocardiogram by abrupt elevation of the ba e line when the current of injury is momentarily abolished by spread of the accession wave through the healthy tissue for such activation causes the healthy tissue to take up a negative potential and so abolishes the potential differences set up by the injury In other words superficial injury results in elevation of the RS T segment In anterior infarcts this displacement is seen in leads V_3-V_6 and is commonly transmitted to V_L and hence to standard lead I (fig 3 20) In posterior infarcts it is seen in low œsophageal leads in V_7 and is transmitted to V_F and hence to standard lead III (fig 3 21)

This classic theory has been challenged by Prinzmetal (1954) on the grounds that intramural electrodes from healthy myocardium adjacent to a fresh infarct do not show depression of the S T segment as they should do if there is a current of injury flowing across the boundary zone from the electrically negative injured tissue to electrically positive healthy muscle instead the S T segment from adjacent areas is normal Again the S T segment from surface electrodes overlying a subendocardial infarct is

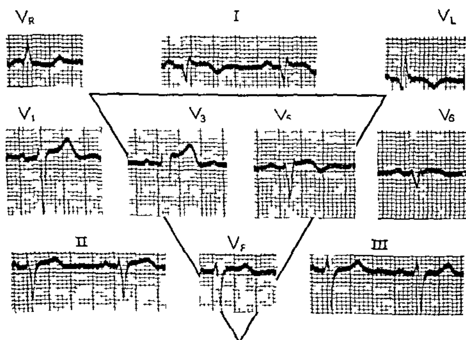


Fig 3 ·4—Anterior myocardial infarction showing an R wave which is smaller in V_3 to V_5 than in V_1

normal not depressed Elevation of the S T segment is always recorded when the intramural electrode is situated anywhere within the injured zone and is maximum at the centre Reciprocal depression occurs over the opposite wall of the ventricle

Pathological Q waves may be seen in acute cases within a few hours of the onset and usually outlast all other evidence of infarction often being permanent Elevation of the RS T segment occurs even earlier, but usually subsides within two or three weeks The shape of the segment is typical being straight instead of concave when initially elevated and being convex or cove shaped (Pardee 1920) when the RS T junction approaches or regains the iso potential level The T wave itself becomes inverted within a few days of the onset often profoundly so, reaching its greatest amplitude at about the same time that the RS T junction first regains the iso potential level (fig 3 23 a and b) Further changes are regressive but the appearances rarely revert to normal

In T_1 patterns reciprocal effects are usually observed in lead III i e the RS T segment may be depressed at first and T may be sharply upright later Again in posterior infarcts early RS T depression and later accentuation of the T wave may often be seen in lead 1 and in anterior chest leads A helpful sign of old anterior infarction is an R wave in V_1–V_2 which is taller than that in V_3–V_4 (fig 3 24) especially when the appearances in V_5–V_6 are more or less normal Finally it is most important to understand that characteristic changes may be found in multiple chest leads or in an œsophageal lead when the standard limb leads are normal and that a single chest lead may be normal when others show diagnostic features

Pericarditis In all types of generalised pericardial disease except hydro pericardium superficial epicardial involvement may cause a current of injury to flow from the surface towards the underlying healthy muscle in other words the surface of the heart develops a negative potential The situation therefore resembles that in superficial myocardial infarction but the lesion is general instead of local Thus in the initial stages elevation of the RS T segment may be seen in all chest leads, in both V_L and V_F and therefore in all standard leads (fig 3 25a) Unlike most records of acute myocardial infarction the RS T segment remains concave As the underlying muscle is healthy there are no pathological Q waves After a few days the RS T segment regains the iso potential level and the T wave becomes inverted (fig 3 25b) Upward coving of the RS T segment does not occur If pericarditis is localised the changes described may be confined to corresponding leads but few important forms of pericarditis remain localised for long Serial records nearly always reveal what may be called the T_{II} pattern in contrast to the T_I or T_{III} types of myocardial infarction Low voltage QRS complexes usually indicate pericardial effusion The electrocardiogram returns to normal as the pericarditis recovers

In *chronic constrictive pericarditis* flattened or inverted T waves

(a) Early stage showing elevation of the RS T segment in leads V_4–V_6, V_F and all standard leads

(b) Late stage showing inversion of the T wave in all standard leads

Fig. 3.25—Pericarditis

leads are permanent and are usually associated with low voltage QRS complexes (fig 3 26) Not infrequently the P waves are widened and relatively prominent

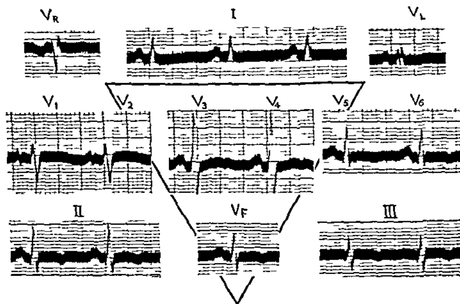


Fig 3 26—Chronic constrictive pericarditis showing low voltage and flat T waves

Digitalis T wave pattern

Digitalis depresses the RS T segment and shortens the Q T interval At first the RS T junction is depressed and there is gentle sagging of the RS T segment T remaining upright (fig 3 27a) In the second stage sagging is more marked and the peak of T can no longer be discerned In extreme digitalisation the RS-T segment becomes a straight line sloping downwards from its depressed origin to a blunt peak (fig 3 27b)

In normal hearts these effects are seen in all leads but especially in lead V_5 and standard lead II When the heart is electrically horizontal they are seen best in V_5 V_L and standard lead I when it is electrically vertical they are best seen in V_5 V_F and standard lead III When the left ventricle is enlarged and the heart horizontal the changes occur more markedly in V_5 V_L and standard lead I and the RS T segment may be elevated and upwardly convex in V_1 V_F and standard lead III When the right ventricle is enlarged they may be most conspicuous in V_1 V_F and standard lead III and the RS T segment may be elevated and upwardly convex in V_5 V_L and standard lead I

Anoxic T waves

Electrocardiograms taken from patients during an attack of angina pectoris may show transient depression of the RS T segment (fig 3 28)

(a) Showing sagging of the RS T segment and shortening of Q Tc to 0 33 second

(b) Showing gross depression of the RS T segment or an inverted T wave with a straight proximal limb Q Tc is shortened to 0 36 second

Fig 3 7—The affect of digitalis on the electrocardiogram (a) slight (b) marked

Fig 3 28—Depression of the RS T segment during an attack of angina pectoris

with or without inversion of the U wave (fig 3 29) Similar records may be associated with carbon monoxide poisoning vasomotor syncope asphyxia and severe hæmorrhage In all these conditions there is myocardial hypoxia *In carbon monoxide poisoning the changes may last for a week or two and* there may be true T wave inversion (fig 3 30) Transient depression of the RS T segment in all leads may be induced in many normal individuals and especially in those with ischæmic heart disease by causing them to breathe 10 per cent oxygen (Levy *et al* 1938) Exertion may have a similar effect in patients with angina pectoris The depression has been attributed to a steady current of injury flowing from the inner layers of the myocardium towards the surface so that the base line of the electrocardiogram is positively displaced When the electrical field is momentarily abolished by the spread of the accession wave the base line temporarily subsides to its



Fig 3 29—Inversion of the U wave during an attack of angina pectoris

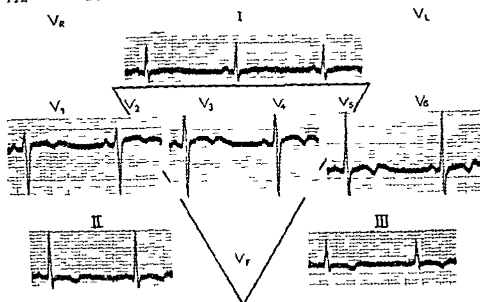


Fig 3 30—Carbon monoxide poisoning

normal level resulting in depression of the S T segment Impairment of coronary blood flow leading to anoxic injury is supposed to be maximal in the deeper layers of the myocardium because the intra myocardial pressure is highest in this situation so that there is no coronary flow during systole, *near the surface coronary flow continues during systole* and so insures a better supply of oxygen to the superficial myocardium

According to Prinzmetal (1954) however ischæmic depression of the S T segment is more likely to be due to functional changes in the outer layers of the myocardium

Permanent depression of the RS T segment in left ventricular surface leads or their equivalents may be seen in a minority of cases with severe ischæmic heart disease and in some cases of severe chronic anæmia In the latter the QRS voltage is usually lowered

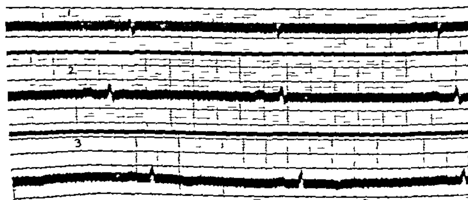


Fig 3 31—Myxœdema

Myxœdema pattern Flat or inverted T waves in all leads are characteristic of myxœdema (fig 3 31) In such cases the voltage of QRS is usually below 6 millimetres in the most favourable standard lead and there is often bradycardia Similar appearances may be found in chronic constrictive pericarditis in long standing cases of severe anæmia particularly pernicious and in anoxic chronic pulmonary heart disease but in these there is commonly tachycardia In severe cases of ischæmic heart disease with

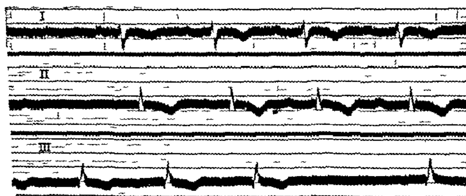


Fig 3 32—Pneumonic carditis There is partial heart block with dropped beats and inversion of the T wave in all leads

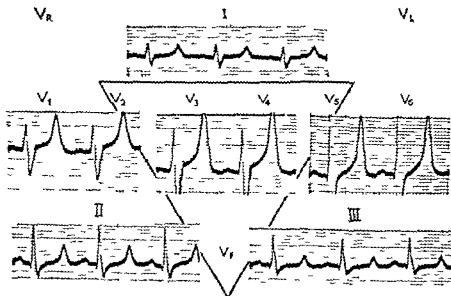


Fig 3 33—High voltage sharply peaked T waves in uræmia associated with a high blood potassium The long Q T interval is due to hypocalcæmia Widening of QRS due potassium is well seen in the chest leads

repeated myocardial infarction somewhat similar graphs may be encountered Indeed, when the whole heart is involved in any disease and when recurrent heart failure has occurred the voltage of QRS may be low and the T waves flat or slightly inverted in all leads, whatever the etiology

Carditis pattern

In any form of carditis but especially in diphtheria and least frequently in acute rheumatism, simple inversion of the T waves may occur and may favour any lead (fig 3 32) The RS T segment may be normal or depressed The voltage of QRS is usually normal

Potassium T wave

In uræmia when the blood potassium is high unusually sharp T waves of high voltage are often seen (fig 3 33) Similar T waves may be produced in normal subjects by raising the blood potassium to about 25 mg per cent by giving 10 to 20 G of potassium acetate by mouth * A high blood potassium also tends to rectify many forms of inverted T wave (fig 3 34) but not those due to myocardial infarction which may be exaggerated

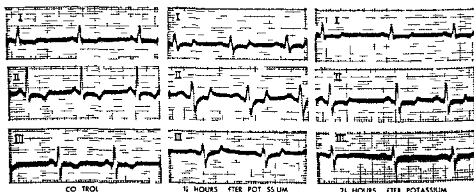


Fig 3 34—Effect of potassium on the T waves in a case of concordant left ventricular preponderance The QRS complex is also widened

(Sharpey Schafer 1943) Widening of P and QRS is also due to potassium and is seen in both illustrations

When the blood potassium is unduly low (<12 mg per cent) the S T segment and T wave may be depressed and the P R interval and Q T_C prolonged (Perelson and Cosby 1949)

* This procedure is dangerous

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CHAPTER IV

RADIOGRAPHIC DIAGNOSIS

TECHNIQUE

THERE are at present six radiological methods applicable to cardiology fluoroscopy orthodiagraphy teleradiography kymography tomography, and angiocardiography Fluoroscopy (screening) is a routine diagnostic procedure orthodiagraphy is the construction of a simple tracing of the size and shape of the heart in any specified position as a supplement to fluoroscopy teleradiography is more accurate and should be preferred when facilities permit kymography records the character and amplitude of cardiac pulsation tomography is sectional radiography angiocardiography is the study of individual cardiac chambers or vessels with the aid of intravascular contrast media

FLUOROSCOPY

With modern X ray equipment a remarkably clear view of the heart may be obtained The patient should be stripped to the waist and pressed close to the viewing screen The diaphragm which controls the diameter of the beam emitted from the X ray tube is first opened wide in order to view the thoracic contents as a whole In this preliminary survey attention is paid to the lungs to the costo phrenic angles and to the general size and shape of the heart The diaphragm is then constricted so that only the heart can be seen and the latter is observed more critically The size shape and pulsation of each part should be noted in regular sequence On the right side (fig 4 01) a faint slightly concave line, representing the superior vena cava descends from the sterno clavicular region close to the shadow of the vertebral column until it meets the ascending aorta which both displaces it to the right and causes it to become convex Below is the border of the right atrium which usually meets the diaphragm at a slightly acute

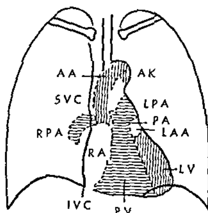


Fig 4 01—Diagram of postero anterior view of the heart as seen fluoroscopically

AA A e d g rt
AK A rt kn kl
IVC I f
LAA L f n l pp d g
LV Left tri l
PA Pulm ry art ry
RA R ght t m
RV R ght nt l
SVC S p a

angle The left border of the normal heart is made up of three convex curves from above downwards these are the aortic knob or knuckle the pulmonary arc, and the contour of the left ventricle Between the last two there is a small neutral segment or point of opposing movement which marks the left atrial appendage above it the pulmonary artery expands during systole while below the left ventricle contracts The hilar shadows are chiefly vascular the right pulmonary artery may be seen dividing early into upper and lower branches the former being indistinct the latter *sweeping* downwards in a well defined arc the left limb of the pulmonary artery forms the main pulmonary arc described above

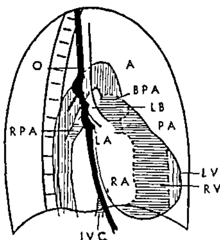


Fig 4 02 (a)—Diagram of right anterior oblique view of the heart as seen fluoroscopically (1st oblique position)

A	A rt c rch
B P A	B furc t on of th pulmo ry artery
I V C	I f io v n c
L A	L ft atr um
L B	L ft b on hus
P A	Pulmon ry ar
O	Bar um filled œsoph g

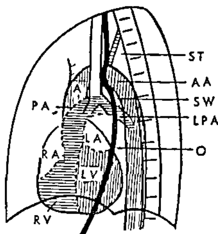


Fig 4 02 (b)—Diagram of left anterior oblique view of the heart as seen fluoroscopically (2nd oblique position)

L P A	Left pulmo ry rt y
L V	L ft nt l
R A	R ght tr um
R P A	R ght pulmo ry t ry
R V	R ght v ntr l
S T	Sup o t t ngl
S W	S b ao t w ndow

The patient is then turned into the first or right anterior oblique position The observer should place his gloved hands on the patient s hips and manually rotate him (so that the right shoulder is brought to the front) until the position is satisfactory The arms should be extended the left forwards and outwards the right backwards and outwards In this view (fig 4 02a) the ventricular shadows are superimposed and the right atrium is rotated towards the front so that little can be learned about these three chambers on the other hand the left atrium is outlined clearly as it forms the upper part of the posterior border of the heart Just anterior to the top of the left atrial curve a rather dense round shadow may be seen due to the bifurcation of the pulmonary artery it is connected with the anterior

ventricular border by a convex line representing the root of the pulmonary artery and conus of the right ventricle Above it are the superimposed shadows of the ascending and descending parts of the aortic arch If the patient is made to swallow a barium emulsion of the consistency of thick cream the œsophagus is outlined at the back of the heart under favourable conditions it is indented in turn by the arch of the aorta by the pulmonary artery and left bronchus and by the left atrium The left bronchus may be seen between the œsophagus and the rounded shadow of the dividing pul monary artery Between the œsophagus and the vertebral column there should be a translucent space

In the second or left anterior oblique position (fig 4 02b) the patient is turned to the right through an angle of about 45 degrees, the left shoulder being brought forwards In this view the two ventricles appear side by side the left forming the posterior border of the heart shadow and the right the anterior so that their contours can be readily compared The shadow of the right atrium overlaps that of the right ventricle the shadow of the left atrium lies posteriorly above the left ventricle Cranially the aorta and pulmonary artery may be seen as two arches one above the other separated by a light space known as the sub aortic window and crossed by the translucent trachea and left bronchus The aortic arch and descend ing aorta are well defined and shaped like an inverted J but the pulmonary artery is less distinct Above the aorta is another light space the supra aortic triangle bounded by the vertebral column posteriorly by the left subclavian artery anteriorly and by the aortic arch below The barium filled œsophagus is deflected to the patient s right as it crosses the aortic arch then lies in close relation to a short segment of the descending aorta leaves that vessel at about the level of the pulmonary artery and courses downwards and to the subject s right across the shadow of the left ventricle

ORTHODIAGRAPHY

Clips should be fitted to the viewing screen to enable tracing paper to be held firmly in position To make an accurate tracing of the heart shadow or orthodiagram special attention should be paid to five points First the position of the patient must be properly adjusted to the view required he must be pressed firmly against the screen and he should hold on to some support so that he can remain still Second the tracing should be made in mid inspiration and as it cannot be completed in one period of breath holding lines which move with respiration should be checked more than once Third to avoid distortion the cardiac outline must be traced by means of parallel rays this is accomplished by constricting the diaphragm to the smallest aperture consistent with adequate visualisation Fourth the greatest accuracy must be maintained when tracing the interior thoracic wall at its widest point and the lateral borders of the cardiac shadow so that the cardio thoracic ratio is reliable Fifth the finished

orthodiagram should be checked against the shadows traced to make sure the patient has not moved during the procedure

Fluoroscopes suitable for cardioscopy are so constructed that the X ray tube may be moved easily in any direction by the lever which operates the diaphragm In making the tracing the small light spot is run swiftly over the contours of the heart great vessels clavicles interior thoracic wall and diaphragm With experience it may be completed very quickly without danger of over exposing the patient or over heating the tube nevertheless a good technician switches off the current whenever momentarily dis engaged Fluoroscopy and orthodiagraphy are usually carried out with a power of 60 kilovolts and a current of 3 to 4 milliamps but with obese subjects it may be necessary to step up the kilovolts to 65 or 70 in order to obtain sufficient penetration Tracings are made with a wax pencil and it is helpful to add signs denoting the degree and direction of pulsation of important chambers and vessels

TELERADIOGRAPHY

Skiagrams of the heart are always taken at a tube screen distance of at least 6 feet preferably 7 feet to avoid distortion by diverging rays The duration of exposure used to be half a second to ensure a diastolic record nowdays however it is commonly 0 1 second and this has introduced a source of error in interpreting serial skiagrams for one may be taken in systole another in diastole and the difference between the two may be appreciable The difficulty may be overcome by using a device whereby one of the electrocardiographic complexes such as R determines the moment of exposure Skiagrams of the oblique views are best taken when the most informative degree of rotation has been ascertained by previous fluoroscopy The normal appearances are illustrated in figure 4 03

KYMOGRAPHY

A specially constructed kymograph may be attached to a teleradiograph for the purpose of recording cardiac pulsation (Stumpf 1931) A lead screen containing horizontal slits 11 mm apart is interposed between the film and the patient s chest and made to descend 1 cm during one com plete cardiac cycle The timing of the exposure is adjusted to synchronise with the descent of the grid In kymograms so obtained the lateral borders of the heart and great vessels appear toothed like the edge of a saw (fig 4 04) the ventricular crests representing diastole the troughs systole Pul sation is recorded in only one dimension i e in a plane parallel to the film but if the three standard views are photographed, the records are sufficiently comprehensive

The electrokymograph is a device for securing an accurate graphic record of pulsation at any point on the cardiac border (Henny and Boone 1947) A photosensitive pick up unit is placed between the patient and the screen so that the lead slit aperture lies across the border of the

heart at the point where it is desired to record pulsation The amount of light transmitted through the aperture varies with the movements of the cardiac border, and is recorded graphically by means of a galvanometer operated by the photo electric cell (fig 4 05) The interpretation of the graph is assisted by a simultaneous jugular phlebogram or electrocardiogram

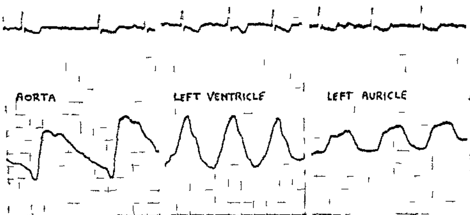


Fig 4 05—Electrokymogram from aorta left ventricle and left atrium in a case of mitral stenosis and incompetence with auricular fibrillation

Neither kymography nor electrokymography have fulfilled earlier expectations The former is too crude to be helpful and the latter too dependent upon the precise position of the slit in relation to the cardiac border being studied so that minor variations in the relationship may alter the graph profoundly

TOMOGRAPHY

Body section radiography was introduced by Ziedses Des Plantes (1932) and others working independently to give radiological information about the lung and major bronchi when these were obscured by thoracoplasty pleural effusion or other large space filling lesion The technique was developed in Berlin by Chaoul and Grossmann (1935) and consists essentially of an arrangement whereby the X ray tube and film move through an arc in opposite directions during the period of exposure Only the plane focused is seen sharply structures anterior or posterior to it being blurred

Although tomography has been used very little in cardiology it may be helpful in demonstrating coarctation of the aorta (Twining 1937) calcified valves (Davies and Steiner 1949) metallic foreign bodies in the heart arteriovenous aneurysm of the lung and anomalous pulmonary veins It

is also helpful in distinguishing dilatation or aneurysm of the pulmonary artery or aorta from other mediastinal masses

Horizontal body section radiography has been used effectively by Stevenson (1950) to demonstrate a double aortic arch and other lesions or anomalies of the aorta

ANGIOCARDIOGRAPHY

If a sufficient quantity of a radio opaque solution is introduced rapidly into the venous circulation its consecutive passage through the right heart pulmonary circulation left heart aorta and major arteries may be recorded by means of serial skiagrams (Castellanos *et al* 1938) The technique was elaborated by Robb and Steinberg (1938 1939) who used 20 to 60 ml of 70 per cent aqueous solution of diodrast A mechanical rapid casette changer enabled serial skiagrams to be taken at a rate of two per second (Sussman Steinberg and Grishman 1941) others preferred serial fluoro photographs obtained by means of a special camera or cinematograph (Stewart Breimer and Maier 1941)

At the time of writing the best contrast medium is a 70 per cent solution of diaginol the sodium salt of 3 acetylamino 2 4 6 triiodobenzoic acid which contains 66 per cent of iodine Patients are best lying down and should be given a preliminary dose of 1 ml to test for hypersensitivity if there is no urticarial reaction within half an hour serious hypersensitivity to iodine is unlikely Premedication varies in different clinics but a com bination of omnopon gr 1/6 to 1/3 or pethidine 50 to 100 mg and the



Fig 4 06—Normal angiocardiogram of right heart postero anterior view



Fig 4 07—Normal angiocardiogram of the right side of the heart second oblique position

anti histaminic phenergan 25 to 50 mg has proved satisfactory the latter is an additional sedative and combats both hypersensitivity reactions to iodine and vomiting from omnopon or pethidine Chlorpromazine is too strong a vasodilator An anaesthetic apparatus for delivering oxygen *under positive pressure should always* be available in cyanotic cases of congenital heart disease and adrenalin should be handy in cases of serious hypersensitivity



Fig 4 08—Angiocardiogram showing pulmonary veins and left atrium

A good cannula 6 to 9 inches long may be made from wide bore polythene tubing This is inserted into the antecubital vein and tied in position the proximal end being connected temporarily with a saline drip or simple syringe When all is ready 30 to 50 ml of diaginol warmed to blood heat is drawn into a strong 50 ml syringe and injected through *the cannula as rapidly as possible preferably in about two seconds*

Modern angiocardiographs are designed to take serial films at a rate of about four per second in postero anterior and lateral views simultaneously The right atrium is usually well filled 1 5 seconds after the start of the

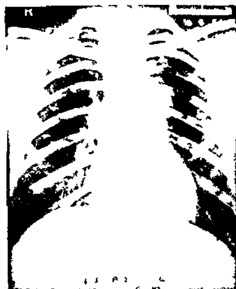


(a) Postero anterior



(b) Second oblique

Fig 4 09—Normal angiocardiograms of the left side of the heart



(a) Skiagram showing a mass between the aortic knuckle and the pulmonary artery

injection the right ventricle and pulmonary artery in 2 to 3 seconds the left atrium in about 5 seconds and the left ventricle and aorta in 6 to 9 seconds (figs 4 06 to 4 09)

The patient experiences a sensation of extreme heat but it passes rapidly The arrival of contrast medium in the lungs may excite a cough and nausea may follow The chief dangers however, apart from hypersensitivity to iodine are syncope due to a sharp fall in blood pressure resulting from general vasodilatation as recorded by Howarth (1950) sudden respiratory arrest and bronchospasm The combination of these adverse reactions may prove rapidly fatal in cyanotic cases of congenital heart disease for they may result in profound anoxia and secondary collapse of the basal centres Dangerous interference with the coronary circulation may also result from the sharp fall in blood pressure (Lawson 1945) The



Angiocardiogram showing normal pulmonary arteries distinct from the mass



(c) Angiocardiogram showing normal aorta d from the mass

Fig 4 10—Angiocardiographic proof that a mediastinal shadow was extra vascular

total mortality rate amongst 6 824 angiocardiographic examinations collected from the main investigatory clinics of the U S A Canada Great Britain and Sweden by Dotter and Jackson (1950) was 0 38 per cent The best treatment for acute pulmonary œdema due to iodine sensitivity is intravenous hydrocortisone

The amount of skin irradiation received by the patient during angio cardiography may be calculated when it is known that about 100 roentgen units are delivered by an X ray tube with the anode set at 90 cm from the skin and operating at 75 kV for 3000 mA second For example at this distance and power 100 r units would be delivered if the patient were exposed for 10 seconds at 300 mA Thus in angiocardiography if each film is exposed for 0 04 second and the tube is operated at 75 kV 450 mA and at a distance of 90 cm from the skin a series of 40 films would result in the patient receiving a skin dose of 25 r units When patients are screened X rayed frequently catheterised and angiocardiographed in two planes simultaneously considerable care must be taken to make sure they are not over exposed The maximum safe dose is 100 r in a week 200 r in a month and 300 r in a year but is *not repeatable*

Angiocardiography has proved especially helpful in establishing the diagnosis of congenital heart disease with right to left shunt e g Fallot s tetralogy pulmonary stenosis with reversed inter atrial shunt pulmonary hypertension with reversed shunt tricuspid atresia and transposition of the great vessels in demonstrating coarctation of the aorta in distinguish ing aneursym of the aorta or pulmonary artery from other mediastinal masses (fig 4 10) and pericardial effusion from cardiac dilatation and in showing the site of superior vena cava obstruction The subject has been well reviewed by Dotter and Steinberg (1951)

SELECTIVE ANGIOCARDIOGRAPHY

Diaginol may be introduced directly into any part of the circulation that can be reached with a relatively wide bore catheter or needle As a rule complete angiocardiograms are more informative but under certain cir cumstances there may be great advantage in the selective technique for example if diaginol is introduced into the right ventricle and arrives immediately in the aorta it must have done so via a ventricular septal defect or because of transposition not via an atrial septal defect or foramen ovale

RETROGRADE AORTOGRAPHY

Diaginol may also be introduced directly into the aorta via a catheter passed up the radial artery To overcome the resistance of the catheter which cannot be of very wide bore a special crusher has been designed by means of a long lever great force can be applied to the plunger of the syringe Retrograde aortography has been of value in demonstrating

coarctation of the aorta (fig 4 11) Good aortograms may be obtained in infants by forcibly injecting 5 ml of contrast medium into the brachial artery through a No 18 needle (Keith and Forsyth 1950) Diaginol may also be introduced into the aorta via a catheter inserted into the femoral artery or directly by needle puncture from behind (Dos Santos 1933 and 1937)



Fig 4 11—Retrograde aortogram showing coarctation of the aorta

Some risk is attached to these procedures Thus temporary hemiplegia has resulted when diodrast has been injected inadvertently into the common carotid artery (Peirce 1953) intermittent claudication in the hand and forearm has followed occlusion of the brachial artery and coronary occlusion is an obvious risk if a catheter is threaded too far down the ascending aorta Nevertheless relatively few complications have been reported and aortography may be helpful at times

CARDIAC MEASUREMENTS

Numerous measurements have been elaborated to serve as indices of enlargement of the heart or of one or more of its chambers but they do not compare with expert opinion based on the methods already outlined The most reliable is the cardio thoracic ratio which is the transverse diameter of the heart (fig 4 12) over the widest internal diameter of the thorax and which should not exceed 0 5 In normal adults the transverse diameter of the heart averages 12 2 cm in the male and 11 cm in the female the range being 8 to 14 5 cm (Roesler 1937)

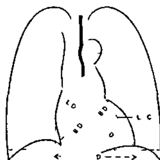


Fig 4 12—Diagram showing the common cardiac measurements

A Width of aorta
B D Broad diameter
L D Long diameter
L V C Left ventricular chord
T D Transverse diameter

The long diameter is measured from the junction of the superior vena cava and right atrium to the apex of the left ventricle and lies between 10 and 15 5 cm averaging 13 cm (Roesler 1937) It is especially increased in cases of left ventricular enlargement but it is also relatively increased in the long narrow heart of asthenic subjects

The broad diameter is the sum of two

perpendiculars drawn from the long diameter to the right cardio phrenic angle below, and to the point of opposing movement on the left border of the heart above and measures 7 to 11 cm in normal adults with an average of 9 cm (Roesler 1937) It may be increased in cases of mitral stenosis and pulmonary heart disease when the transverse and long diameters are normal

The location of the point of opposing movement is important for it tends to be raised or lowered according to whether enlargement is mainly left or right ventricular respectively Similar significance is attached to the length of the chord which subtends the arc of the left ventricle measured from the point of opposing movement to the left cardio phrenic angle this line is normally 6 to 12 5 cm long and averages 9 cm (Roesler 1937)

The antero posterior diameter of the heart is measured from teleradio grams taken in the lateral position and varies between 7 and 11 cm with an average of 9 cm It is a useful check on the significance of an increased transverse diameter for if this is due to cardiac enlargement the antero posterior diameter should be increased proportionately whereas if it is due to depression of the sternum the depth of the heart is decreased The antero posterior diameter is especially increased in mitral stenosis

The width of the aorta (2 to 3 cm) may be measured in the antero posterior or oblique positions whichever presents the clearest view of two sides of the vessel In the anterior view the measurement should be made from the left side of the barium filled œsophagus to the left border of the aortic knuckle but it is only valid when the posterior part of the aortic arch passes directly backwards i e in a direction perpendicular to the frontal plane In the oblique views barium in the œsophagus may also be helpful in the second oblique position for example the œsophagus may be deflected abruptly as it crosses the aorta so that the width of the vessel is seen clearly In practice a normal aorta is most easily measured in the postero anterior view a syphilitic atheromatous or unfolded aorta in the second oblique view

NORMAL VARIATIONS

Both the size and shape of the heart vary greatly in normal individuals thus in children and adolescents the pulmonary artery may be relatively prominent (fig 4 13) in lean asthenic subjects the heart may be elongated and central in position (fig 4 14) in short stocky individuals it is apt to lie transversely (fig 4 15) rarely the left atrium can be seen in the P A view (fig 4 16)

Displacement or rotation of the heart to left or right is often due to coliosis the common finding being displacement of the heart to the left the spinal curvature being convex to the right Rotation of the spine with out conspicuous lateral curvature may cause considerable displacement or rotation of the heart When cardiac displacement is due to partial collapse



Fig 4 13—Telera lıogran t hıld showıng relatıve pr ı n n t ı th pulmon ırı ıt r



F ı 4 14—The elongated centrally placed heart of a lean asthenic subject



Fig 4 15—Transversely placed heart of a short stocky subject



Fig 4 16—Skiagram of a normal heart in hich the border of the left atrium is seen on the right side between the superior ver cava and the right atrium

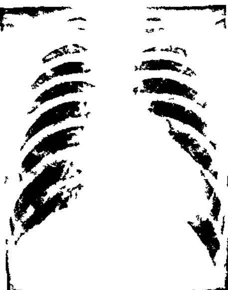


Fig 4 17—Displacement of the heart to the left without obvious cause



Fig 4 18—Displacement of the heart to the right attributed to old mediastinal pleurisy



Fig 4 19—Enlargement of the heart due to sinus brady cardia



Fig 4 20—Teleradiogram of an obese subject showing a triangular opacity at the apex of the heart (pericardial fat)

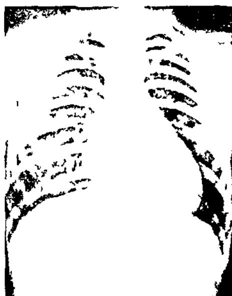


Fig 4 21—Apparent enlargement of the heart in a case of depressed sternum



(a) The heart in diastole



(b) The heart in systole

Fig 4 22—Teleradiograms of the same patient taken with short exposures showing difference in size of heart shadow in diastole and systole

of the lung increased translucency of the over expanded normal lung on the same side is usually observed and is a valuable sign when the collapsed part cannot be seen Occasionally the heart may be displaced to left or right without obvious cause (figs 4 17 and 4 18) Mediastinal pleural adhesions can be demonstrated in some of these cases (Kerley 1954)

Slight enlargement particularly of the left ventricle and of the transverse diameter is often seen in patients with slow heart rates whether due to sinus bradycardia, sino auricular block or to heart block The enlargement depends upon increased diastolic filling the slow rate being compensated by a large stroke volume (fig 4 19) Slight enlargement of similar type may be encountered in athletes in some it may be explained by sinus bradycardia which is common in these subjects but in others it may be due to the extra demands which have been made on the heart

In obese subjects the left cardio phrenic angle may be filled out by a triangular pad of fat (fig 4 20) this must not be confused with left ven tricular enlargement In cases of depressed sternum the postero anterior skiagram may reveal general enlargement of the heart shadow but in the oblique views the depth of the heart is seen to be correspondingly reduced (fig 4 21)

When such causes can be excluded and unsuspected enlargement of the cardiac silhouette is revealed by a skiagram it is wise to check the tech nique employed Portable X rays or pictures taken with the patient lying or sitting may be misleading owing to distortion Short exposures may catch the heart in systole and a skiagram so obtained may be appreciably smaller than one photographed in diastole (fig 4 22)

The heart may be smaller than normal in many wasting diseases when atrophy takes place but this is of little practical importance

RADIOGRAPHIC ABNORMALITIES

Some of the illustrations referable to this section may be found in other chapters but for the sake of convenience are reproduced here

ABNORMALITIES OF THE AORTA

Saccular aneurysm (fig 4 23 a and b) is pathognomonic of syphilis It may be distinguished from other space filling lesions by its intimate con nexion with the aorta in all views by calcification of its walls and by its pulsation a thrombosed sac however, may not pulsate Angiocardiography is helpful in doubtful cases Fusiform aneurysm (fig 4 24) usually means syphilitic aortic incompetence but may also be due to dissection and when confined to the ascending aorta to congenital hypoplasia both these conditions may also be complicated by aortic incompetence Fusiform aneurysm should be distinguished from prominence of the ascending aorta due to aortic stenosis or incompetence of any etiology (fig 4 25) Syphilitic aortitis without aneurysm or fusiform dilatation can only be diagno



(a) Anterior view



(b) Second oblique position

Fig 4 23—Saccular aneurysm of the aorta
(By [illegible] J h Park[illegible]on)



(a) Postero-anterior view



(b) 2nd oblique position

Fig 4 24—Fusiform aneurysm of aorta

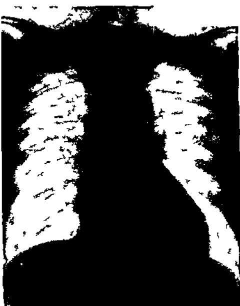


Fig 4 5—Prominence of the aorta due to rheumatic aortic incompetence



Fig 4 26—Unfolding of the aorta in hyper tensive heart disease



Fig 4 2 —Unfolding of the aortic arch illus trated by barium in the œsophagus

radiologically if inequalities of outline can be clearly demonstrated e g by means of angio cardiography

Unfolding of the aorta may occur in aortic valve disease in hypertensive heart disease and in atherosclerosis The ascending limb is con spicuous the knuckle is unduly prominent and the descending limb appears to the patient s left in the postero anterior view (fig 4 26) In the second oblique position the arch is wider than normal and its posterior part may pull the œsophagus backwards (fig 4 27) Vigorous pulsation proclaims aortic incompetence rather than hypertension or atherosclerosis

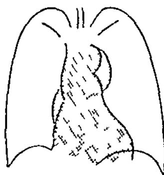


Fig 4 28 — Orthodiagram illustrating tortuosity of the aorta

Tortuosity of the aorta is characteristic of atherosclerosis it is best seen in the second oblique view but may be so marked that the descending limb appears to the right of the heart shadow in the postero anterior view (fig 4 28) Calcification of the aorta is of four main types (1) calcification of the ascending aorta is practically diagnostic of syphilis (2) a comma shaped calcified plaque in the aortic knuckle is characteristic of atherosclerosis (3) calcification outlining irregularities in the wall of the thoracic aorta in any position means syphilis (fig 4 29) (4) calcium is frequently laid down in the wall of a saccular aneurysm



Fig 4 29—Irregular calcification of the aortic arch in a case of syphilitic aortitis

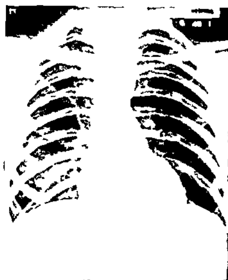


Fig 4 30—Coarctation of the aorta showing a prominent left subclavian artery elongated aortic knuckle post stenotic dilatation of a short segment of the descending aorta above the pulmonary arc rib notching and fullness of the left ventricle

Coarctation of the aorta may be recognised by the prominent left subclavian artery elongated aortic knuckle and post stenotic dilatation of a short segment of the descending *aorta (fig 4 30)* the *diagnosis is confirmed* by rib notching and enlargement of the left ventricle and denied by appearances indicating unfolding of the aorta

A right sided aortic arch is seen occasionally as an isolated *congenital* anomaly but more often it is associated with Fallot s tetralogy or Eisenmenger s complex The aortic knuckle projects to the patient s right and the barium filled œsophagus is deflected to the left (fig 4 31)

Hypoplasia of the aorta is rare as a solitary congenital abnormality but is common in association with certain other congenital or acquired lesions especially atrial septal defect and mitral stenosis The aortic knuckle is small and its pulsation diminished



(a) Anterior view



(b) First oblique position

Fig 4 31—Right s ded aortic arch illustrated by means of barium in the œsophagus
(By courtesy of J S J h Parkes)

ABNORMALITIES OF THE LEFT VENTRICLE

Left ventricular enlargement is encountered chiefly *in hypertensive heart* disease aortic valve disease patent ductus arteriosus and organic mitral incompetence but may occur in various conditions as part of general enlargement It is easily recognised by the *density and bulk of the left* ventricular shadow in the postero anterior and second oblique positions by increase in the transverse and long diameters of the heart and th



Fig 4 32—Enlargement of the left ventricle due to aortic stenosis



Fig 4 33— Pulmonary venous congestion and bilateral hydrothorax from left ventricle failure



Fig 4 34—Left ventricular aneurysm



Fig 4 35—Calcified left ventricular aneurysm
(*With acknowledgments to Dr* [illegible])

left ventricular chord and by elevation of the point of opposing movement In hypertension and aortic valve disease the shadows of the unfolded aorta and of the heart itself may be compared either to two ovals set at right angles, or to the shape of a boot (fig 4 32)

When there is left ventricular failure (fig 4 33) the hilar shadows are exaggerated a fan shaped opacity appears at the hilum representing interstitial œdema and softer mottling spreads outward towards the periphery when there is pulmonary œdema Hydrothorax may be present and if unilateral is usually left sided (Bedford and Lovibond 1941)

Left ventricular aneurysm may present as a bulge on the left border of the heart usually towards the apex (fig 4 34) and may exhibit paradoxical pulsation occasionally the wall of the aneurysm is calcified (fig 4 35) Myocardial infarction may be located with precision in some cases by the fluoroscopic demonstration of an area with absent or paradoxical pulsation

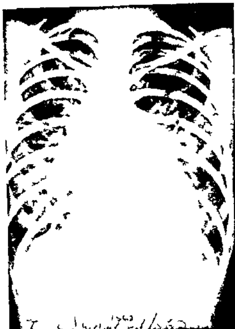
DILATATION OF THE LEFT ATRIUM

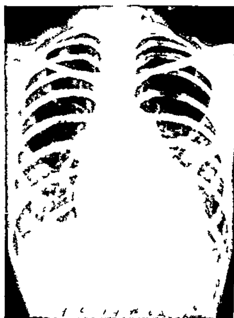
Conspicuous dilatation of the left atrium invariably means organic mitral valve disease but the chamber may be unduly full in cases of left ventricular failure In the postero anterior view it may appear as a bump on the left border of the heart between the pulmonary artery and left ventricle (fig 4 36) The proof that this bump represents the left atrium or left atrial appendage rather than the conus of the right ventricle is as follows (1) it is only seen in cases of mitral valve disease when it is related to the size of the left atrium not to the pulmonary vascular resistance (2) in angiocardiograms it opacifies with the left atrium not with the right ventricle (Grishman Sussman and Steinberg 1944) (3) it contracts with the atria in cases of complete heart block and expands with the rest of the left atrium in cases of severe mitral incompetence (4) it disappears after appendicular resection (fig 4 37) (5) if a catheter is introduced into the left atrium via an atrial septal defect or foramen ovale its tip can nearly always be passed to the very edge of the cardiac border at the site in question whereas in the conus of the right ventricle it is always well medial

On the right border of the heart an enlarged left atrium appears as a



Fig 4 36—Dilatation of the left atrium forming a bump between the pulmonary arc and left ventricle in a case of organic mitral incompetence





(a) (b)

Fig 4 37—Skiagram of a case of mitral stenosis showing (a) intense pulmonary venous congestion dilatation of the pulmonary artery and left atrium before operation and (b) disappearance of both the congestion and the left atrial appendage after mitral valvotomy and appendicular resection



Fig 4 38—Dilatation of the left atrium seen on both borders of the heart in the postero anterior view in a case of mitral incompetence



Fig 4 39—Dilatation of the left atrium illustrated by means of barium in the œsophagus Case of mitral stenosis Note the sharp curves produced by the aortic arch and the left bronchus and pulmonary artery



Fig. 4.40— Dilatation of the left atrium in a case of hypertensive heart disease (necropsy proof)

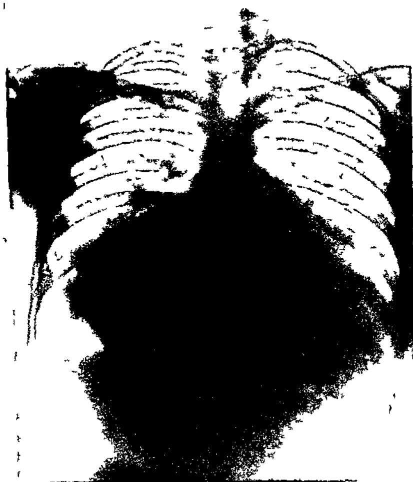


Fig 4 41—Aneurysmal dilatation of the left atrium in a case of mitral valve disease

convex shadow above but overlapping that of the right atrium (fig 4 38) The barium filled œsophagus is usually deflected to the patient s right in the postero anterior view

In the right anterior oblique position the œsophagus is displaced back wards in an abrupt manner immediately below the left bronchus and pul monary artery (fig 4 39) the antero posterior diameter of the heart being increased and the retrocardiac space decreased correspondingly Back ward displacement of the œsophagus from an enlarged left ventricle is rarely so abrupt or so high but on occasions it may be indistinguishable (fig 4 40) In the left anterior oblique position an enlarged left atrium causes the œsophagus to be deflected back wards above the shadow of the left ventricle

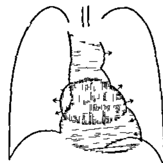


Fig 4 42—Orthodiagram illus trating expansile pulsation of the left atrium during ven tricular systole in a case of organic mitral incompetence

Aneurysmal dilatation of the left atrium (fig 4 41) may be caused by rheumatic mitral incompetence or stenosis but it is probable that a high degree of atrial muscle damage is an important contributory factor

Systolic expansile pulsation of the left atrium is pathognomonic of mitral incom petence usually organic It is especially convincing when seen on both borders of the heart in the postero anterior view (fig 4 42) In the first oblique position back ward pulsation of the left atrium is often seen in mitral stenosis but the quality and amplitude of the movement in organic mitral incompetence are most impressive and are easily recognised with experience

A rare complication of mitral stenosis is calcification of the left atrial endocardium

ABNORMALITIES OF THE PULMONARY ARTERY

DILATATION OF THE PULMONARY ARTERY may be associated with con genital or acquired heart disease and is due to hypoplasia an increased pulmonary blood flow or pulmonary hypertension Congenital causes include idiopathic dilatation of the pulmonary artery pulmonary valve stenosis with normal aortic root patent ductus arteriosus ventricular septal defect atrial septal defect and Eisenmenger s syndrome acquired causes include primary pulmonary hypertension subacute thrombo embolic pulmonary hypertension hypertensive cor pulmonale pulmonary hypertensive mitral stenosis and other varieties of secondary pulmonary hypertension such as schistosomiasis periarteritis and disseminated lupus Slight dilatation of the pulmonary artery may occur in any of the hyper kinetic circulatory states and in passive pulmonary hypertension secondary to chronic left ventricular failure or mitral valve disease

In *idiopathic dilatation* the peripheral pulmonary vessels and the heart

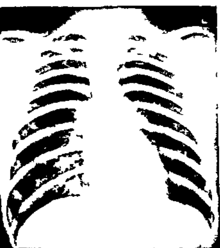


Fig 4 43—Idiopathic dilatation of the pulmonary artery

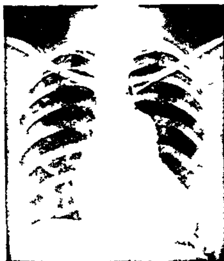


Fig 4.44—Dilatation of the pulmonary artery in a case of pure pulmonary stenosis



Fig 4.45—Dilatation of the pulmonar artery and its branches associated with left ventricular enlargement due to patent ductus

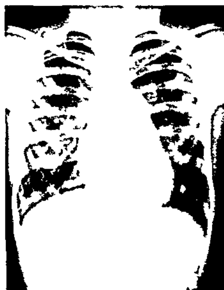


Fig 4.46—Dilatation of the pulmonary artery in a case of Eisenmenger's complex



Fig 4 47—Dilitat n of the pulm nary artery and its branches associated with hypoplasia of the rt and right d d enlargement in a case of atrial septal defect

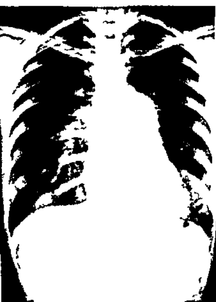


Fig 4 48—Dilatation of the pulmonary artery due to primary or idiopathic pulmonary hypertension



Fig 4 49—Dilatation of the pulmonary artery due to extreme pulmonary hypertension in a case of mitral stenosis



(a) Postero anterior view



(b) First oblique position

Fig 4 50—Dilatation of the pulmonary artery and its main branches in a case of chronic cor pulmonale due to emphysema

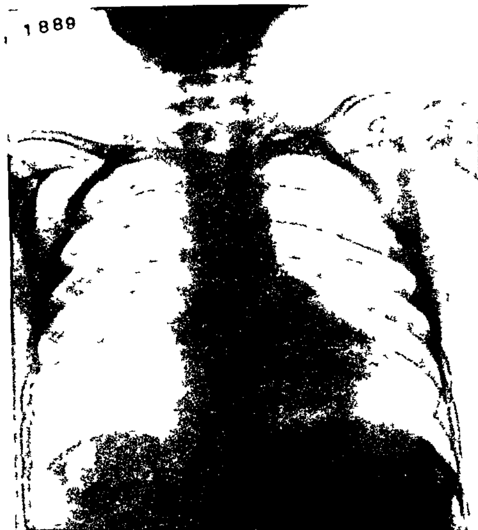


Fig 4 51—The Cœur en sabot due to Fallot s tetralogy

itself are normal (fig 4 43) unless there is secondary pulmonary incompetence when the right ventricle is dilated

In *pulmonary valve stenosis* (fig 4 44) the peripheral vascular markings may be diminished and the right ventricle and atrium enlarged according to the degree of stricture

In *patent ductus* dilatation of the pulmonary artery is due to an increased pulmonary blood flow and is associated with heavy pulmonary vascular markings and enlargement of the left ventricle (fig 4 45) the appearances in *ventricular septal defect* are similar except that the right ventricle is enlarged as well the appearances are also similar in *atrial septal defect* but here only the right ventricle and right atrium are enlarged (fig 4 47)

In *Eisenmenger s syndrome* dilatation of the pulmonary artery is due to pulmonary hypertension the peripheral vascular shadows are normal or light The right ventricle is hypertrophied but not dilated so that the transverse diameter of the heart may be normal (fig 4 46) as in Fallot s tetralogy

Primary pulmonary hypertension is characterised by dilatation of the pulmonary artery with diminished peripheral vascular markings due to pulmonary vasoconstriction and a low cardiac output (fig 4 48) The right ventricle and atrium are enlarged the left ventricle small Appearances are similar in subacute cor pulmonale from thrombo embolism

The degree of dilatation of the pulmonary artery in mitral stenosis is closely related to the pulmonary vascular resistance when this is extreme the radiological appearances may resemble those of primary pulmonary hypertension (fig 4 49)

In hypertensive cor pulmonale radiological evidence of emphysema polycystic lung or diffuse pulmonary fibrosis are added to the picture (fig 4 50)

HYPOPLASIA OF THE PULMONARY ARTERY is characteristic of Fallot s tetralogy (fig 4 51) There may be a distinct gap between the aortic knuckle and the curve of the left ventricle the vascular shadows at the hilum are reduced on both sides and the lung fields are remarkably clear

ENLARGEMENT OF THE RIGHT VENTRICLE

Right ventricular enlargement is more difficult to recognise than left In the postero anterior view there is usually some increase in the transverse and broad diameters the right atrium being pushed a little to the right and the interventricular septum to the left

When hypertrophy of the right ventricle is associated with clockwise rotation of the heart the anterior edge of the septum forms most of the left border of the heart only the tip of the left ventricle being visible beyond it the effect produced is that of increased angularity of the cardiac apex and a more acute left cardiophrenic angle the general shape resembling the Dutch peasant s wooden shoe with turned up toe T



Fig 4 52—Right ventricular enlargement in a case of mitral stenosis (2nd oblique position)

is the coeur en sabot' and is especially characteristic of Fallot s tetralogy (fig 4 51)

When the right ventricle is dilated as well as hypertrophied as in atrial septal defect it may occupy the whole of the left border of the heart and form the apex beat proper in the postero anterior skiagram it is often impossible to be sure which ventricle is responsible for the enlargement and experience has *proved over and over* again that the electrocardiogram is a far more reliable guide

In the left anterior oblique position right ventricular enlargement is recognised by the increased curvature of the anterior border of the heart shadow Instead of the lob sided appearance resulting from normal left ventricular bias the heart shadow is more globular the anterior and posterior ventricular curves being more equal (fig 4 52) If the right atrium is enlarged however as may be determined from the postero anterior view interpretation is more difficult for its shadow is superimposed on that of the right ventricle in the second oblique position and it may be entirely responsible for the increased curvature of the anterior border

The right ventricle is enlarged particularly in pulmonary hypertension pulmonary stenosis pulmonary incompetence and atrial septal defect Hypertrophy rather than dilatation *is characteristic of Fallot s tetralogy* and Eisenmenger s complex dilatation usually means failure from pulmonary hypertension or simple pulmonary stenosis or an increased stroke volume as in atrial septal defect

ENLARGEMENT OF THE RIGHT ATRIUM

Dilatation of the right atrium usually associated with fullness of the superior vena cava is seen in congestive heart failure atrial septal defect severe pulmonary hypertension or stenosis tricuspid stenosis or incompetence and Bernheim s syndrome

As a rule a dilated right atrium is recognised by its relatively low position on the right cardiac border and by the blunt angle it makes with the diaphragm (fig 4 53) When the left atrium appears on the right border of the heart it is higher more rounded, and forms a zone of



Fig 4 53—Gross enlargement of the right atrium due to tricuspid valve disease

CONSTRICTIVE PERICARDITIS

The most important radiological evidence of constrictive pericarditis is loss of pulsation without cardiac enlargement but calcification of the pericardium is common and helpful and is usually best seen in the left anterior oblique position (fig 4 58) Slight to moderate enlargement of the heart shadow may occur if the pericardium is sufficiently thick (1 to 2 cm) but the triangular appearance given by the obliquely set straight right and left borders should suggest the correct diagnosis (fig 4 59)



4 58—Ca of chronic con tricti e peri itis sho ving extens e calcification of the pericardium (2nd oblique pos tion)

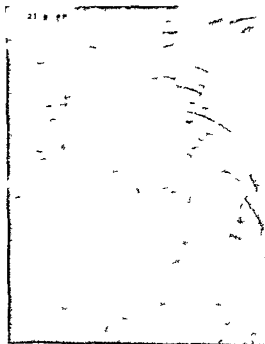


Fig 4 59—Chronic constrictive pericarditis showing triangular shaped heart in the anterior view

CALCIFIED VALVES

Calcified valves are best seen fluoroscopically they may be recorded by means of tomography The patient should be turned 15 degrees to the left and an imaginary line drawn from the point of opposing movement on the left border of the heart downwards and to the patient s right at an angle of 45 degrees with the horizontal (fig 4 60) The aortic valve is situated just above this line in the centre of the heart shadow the mitral just below it and a little to the patient s left Calcification may be recognised by linear or anti clockwise elliptical movement of dense crescentic opacities in the direction of the anatomical axis of the heart synchronous with the heart

beat. The technique requires proper accommodation and maximum constriction of the diaphragm so that only a square inch or so of the screen is visible. Calcified aortic valves are sometimes better seen in the second oblique position where they lie at the intersection of a vertical line through

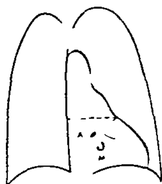


Fig. 4.60—Orthodiagram showing the position of calcified valves. The patient has been turned fifteen degrees to his left.
A. Aortic valve
M. Mitral valve

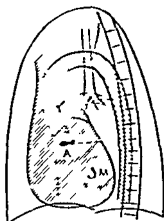


Fig. 4.61—Orthodiagram showing the position of calcified valves in the 2nd oblique position.
A. Aortic valve
M. Mitral valve

the centre of the heart shadow and a horizontal line through the top of the left ventricular arc (fig. 4.61). This view may be helpful in valve differentiation, for the mitral valve lies in the posterior third of the heart shadow and at a lower level (Sosman, 1939).

PULMONARY VASCULAR SHADOWS

Radiological examination of the heart is incomplete without careful inspection of the pulmonary vascular shadows. The normal lung markings are practically all vascular. The heavier shadows are arterial and taper evenly to the periphery.

In severe pulmonary hypertension due to a high pulmonary vascular resistance normal tapering disappears and is replaced by an abrupt change of calibre at a fairly proximal level; the main left and right pulmonary arteries are dense and dilated but the peripheral vessels are spidery and the outer lung fields unduly translucent (fig. 4.48).

Pulmonary ischæmia (or oligæmia) associated with a dilated pulmonary artery is characteristic of severe pulmonary valve stenosis, the diminished pulmonary blood flow being due to a low cardiac output or to reversed interatrial shunt (fig. 4.44).

Pulmonary ischæmia with a hypoplasic pulmonary artery is seen especially in Fallot's tetralogy (fig. 4.51) and tricuspid atresia.

Clear lung fields due to a diminished pulmonary blood flow are also seen in pericardial effusion Ebstein s disease (fig 4 62) and certain other low output states

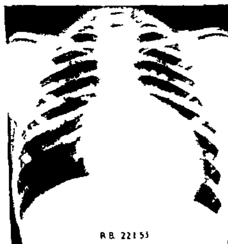


Fig 4 62—Pulmonary ischæmia associated with a low cardiac output in a case of Ebstein s disease the enlarged heart shadow is due to dilatation of the right ventricle and atrium

Pulmonary plethora may be defined as heavy pulmonary vascular markings due to an increased pulmonary blood flow the shadows are peripheral as well as central and are chiefly arterial Pulmonary plethora is seen in patent ductus arteriosus (fig 4 45) aorto pulmonary septal defect ventricular septal defect atrial septal defect (fig 4 46) anomalous pulmonary venous drainage transposition of the great vessels and persistent truncus arteriosus Heavy tapering vascular shadows spread far out into the lungs and in cross section form unusually dense round opacities

Other arterial abnormalities such as arterio venous fistula absence or occlusion of a major pulmonary artery and broncho pulmonary anastamoses are described elsewhere

Pulmonary venous congestion presents as fan shaped mottling spreading out from the hilum on each side (fig 4 37a) and is characteristic of mitral stenosis and left ventricular failure Heavy woolly shadows are superimposed in cases of pulmonary œdema Fine horizontal lines best seen near the right costophrenic angle represent engorged lymphatics (Kerley 1933)

Anomalous pulmonary venous drainage and anomalies of the venæ cavæ are described in Chapter VIII

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CHAPTER V

SPECIAL INVESTIGATIONS

STETHOSCOPIC auscultation sphygmomanometry, ophthalmoscopy, electrocardiography and radiology have become routine technical methods of investigation which are used by the cardiologist before he arrives at his initial clinical diagnosis The techniques described in this chapter have not yet become routine in this country and are unlikely to do so for a precise etiological anatomical and functional diagnosis can usually be made without them and they infrequently reveal anything totally unexpected For the most part they are refinements of simpler techniques—accurate methods of measuring quantity when the quality of something is already known Occasionally they are used to solve a particular qualititative problem

DIRECT MEASUREMENT OF THE VENOUS PRESSURE

Whilst elevation of the venous pressure is usually detected clinically with little difficulty there are occasions when it is valuable to check it by direct measurement (Moritz and Tabora 1910) The subject should be propped up at an angle of 30 to 45 degrees because patients with orthopnœa can not lie flat and the technique should be the same for all cases The right arm bared to the shoulder is abducted to a right angle and supported on pillows so that the antecubital fossa is roughly at heart level An infusion needle connected to a spinal manometer or similar graduated glass tube is then inserted into the antecubital vein the zero mark on the manometer being placed at the level of the fourth costal cartilage by means of a spirit level the height to which blood rises above this mark represents the venous pressure Alternatively the zero mark may be placed at the level of the sternal angle or of some other reference point To avoid clotting a saline reservoir containing a drop of heparin should be attached to the system by means of a T shaped glass connexion as shown in figure 5 01 a few ml of the solution being

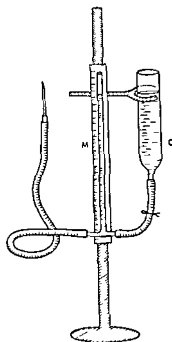


Fig 5 01—Apparatus for measuring the venous pressure
M M nom t r grad ted in cm C C t t or al e rvoir

allowed to flow through from time to time With this modification the manometer contains saline instead of blood The result should be expressed in cm of water (a horizontal line through the fourth costal cartilage with the patient at 45 degrees cuts the superior vena cava just above its junction with the right atrium) or in cm of water above or below the sternal angle If the technique is satisfactory the saline column should rise and fall gently with respiration and should rise sharply when the arm is constricted above the needle The normal venous pressure as so measured, ranges between 2 and 10 cm of water and averages 5 76 cm (Wood 1936) expressed with reference to the sternal angle it may be plus or minus 0 to 3 cm in relatively horizontal positions

In the *phlebomanometer* described by Burch (1950) a 12 cm glass observation tube with a bore of 1 00 mm is attached to the veni puncture needle and is connected by means of rubber tubing to the saline manometer through a three way tap which is also connected to a pneumatic pressure bulb Immediately before use 2 per cent sodium citrate is drawn up through the needle into the observation tube until the meniscus reaches a set mark When the needle is inserted into the vein the positive venous pressure tends to force the meniscus up the observation tube but this tendency is corrected by increasing the pressure in the pneumatic system connecting the tube with the saline manometer (by means of the pressure bulb) The pressure required to keep the meniscus at the mark is the venous pressure

THE JUGULAR PHLEBOGRAM

The polygraph is an instrument for making simultaneous graphic records of two or more vascular pulsations Mackenzie (1902) concentrated on the jugular phlebogram as a means of analysing abnormalities of rhythm The instrument consists essentially of some sort of receiver which is placed over the internal jugular vein to pick up changes in volume or pressure connections to transmit these changes to the recorder an amplifying system to increase the magnitude of the changes and the recorder itself In Mackenzie s *clinical polygraph* which was made by Shaw the receiver was an open shallow cup and was connected pneumatically by means of a rubber tube to a tambour Amplification depended on the length of the lever (usually 6 inches) fixed to the membrane of the tambour The moving end of the lever was arranged to write on smoked paper covering a revolving drum Two or more such systems operated together so that the jugular pulse could be timed against the carotid or radial pulse and against the apex beat The disadvantages of this simple arrangement were the mechanical inertia of the levers the primitive method of recording and the pneumatic time lag

By cementing a small mirror to the membrane of the tambour in an eccentric position Frank (1903) overcame the problem of mechanical inertia *Optical records* were obtained by photographing the movements of

a beam of light reflected from the mirror the length of the beam providing excellent amplification But the *mirror capsule* was still operated by volume displacement in an air system and suffered from the same time lag as Mackenzie s instrument

To overcome this defect the receiver had to be some sort of transducer, i e a device which converts a pressure or volume change into a proportional electrical voltage A *carbon granule microphone* similar to that used in commercial telephony answers the purpose fairly well although it suffers from non linear distortion It consists of two electrodes between which are packed the carbon granules one of the electrodes is movable and is attached to a diaphragm which is displaced by changes in external pressure When the diaphragm is pushed inwards the carbon granules are com pressed decreasing the resistance between the two electrodes A current flowing through the chamber is thus altered by any movement of the diaphragm The current can be led to a suitable galvanometer the movements of which can be recorded as in an electrocardiograph

Piezo electric (πιέζειν to press) *crystal microphones* have also been used with some success (Gomez and Langevin 1937 Miller and White 1941) They depend on the property of certain crystals such as quartz and Rochelle salt (sodium potassium tartrate) to develop electrical charges when subjected to mechanical strain The crystal must be cut in a special way, for it will only respond electrically when pressure is applied to it in a particular direction It is mounted between two electrodes one of them being fixed to a projecting button which can be placed on the jugular vein When the button is pushed in by the jugular pulse the crystal is compressed and electrical charges of equal amplitude and opposite sign proportionate to the stress develop on each side of the crystal these are picked up by the electrodes amplified and led to a suitable galvanometer and recorder

Microphone receivers are designed to be used in conjunction with multichannel recorders so that thermionic valve amplification galvanometer and recording device are already available The transducers themselves have a high frequency response linear in the case of the piezo electric type, and eliminate time lag Unfortunately the changes that develop are so small that no insulator is sufficiently perfect to preserve them for long so that these crystals cannot be used as transducers for electromanometers which are required to measure static and mean pressures

The *jugular phlebogram* is a good qualitative graphic record of what the clinician actually sees at the bedside it is not quantitative and cannot be standardised The venous pulse is said to travel at a rate of 1 to 3 metres per second (Morrow 1900) this means that the delay between right atrial and internal jugular events should lie between 0 15 and 0 05 sec which is rather longer than that found with modern techniques (about 0 05 sec in our own laboratories) In using the phlebogram to help identify phono cardiographic events this venous time lag must be borne in mind

The chief waves of the venous pulse have already been described in detail and are illustrated again in figure 5 02 The onset of *a* is 0 07 sec after the peak of the electrocardiographic P wave which signals the onset of right atrial contraction The prominent *c* wave is typical of jugular

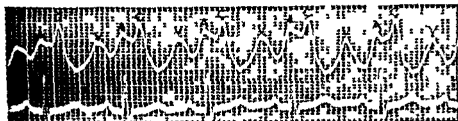


Fig 5 02—Jugular phlebogram

A Atrial contraction
C Carotid pulse
V The summit signals the opening of the tricuspid valve

phlebograms and is due to carotid pulsation The peak of *v* signals the opening of the tricuspid valve when allowance is made for time lag The two troughs are *x* and *y*

THE ARTERIOGRAM

A *sphygmogram* (σφυγμος pulse) is a tracing or graphic record of any kind of pulse and although the original sphygmographs were designed for obtaining arterial pulse tracings and the word pulse customarily means an arterial pulse unless otherwise specified it is better to describe an arterial pulse record as an arteriogram and the procedure arteriography

Arteriograms may be recorded indirectly by placing a receiver over an arterial pulse or directly by inserting a needle into the artery *Indirect arterial sphygmographs* were in common use in the nineteenth century Marey (1863) designed and used an instrument which was of great help to Potain (1867) and in 1902 Mackenzie stated that the construction of these instruments was familiar to all medical men The receiver had a steel spring the foot of which was placed directly over the radial or other arterial pulse a long lever was attached to the spring so that movements were magnified and the lever was made to write on smoked paper The Dudgeon type was perhaps best known in this country Subsequent development has been the same as that described for jugular phlebographs and carbon microphones or piezo electric crystals electrical transmission thermionic valve amplification and electrocardiographic type of galvanometer and recording are now used

In the *direct method* a needle (18 to 20 gauge) is inserted into the brachial or femoral artery and is connected to a suitable manometer by a non elastic plastic or lead tube containing heparinised saline

Manometers

OPTICAL MANOMETERS use the principle of Frank s mirror capsule (q v) In the instrument designed by Hamilton (1934) a 5 mm square 0 5 dioptre plano convex mirror silvered on the plane side was cemented eccentrically to a membrane made of brass 0 06 mm thick, or coin silver 0 0015 inches thick which formed the terminal face of a metal chamber fitted with citrate solution which was connected hydraulically by means of a lead tube to an 18 gauge Luer needle used for arterial puncture A slit lamp was arranged so that a beam of light up to 5 metres long was reflected from the mirror on to moving photographic film or paper The manometer could be standardised by recording the response to known changes of pressure the length of the beam of light being adjusted to the amplification required The response of the manometer was linear and of reasonably high frequency

This type of apparatus can also be used in conjunction with a *photo electric cell* which is influenced by the beam of light reflected from the mirror (Rein *et al* 1940) There are several kinds of photo electric cell, the principles of which may play an increasing part in medical recording devices In the *photo emission cell* a semi cylindrical silver cathode coated on the inside with a photo emitter (such as cæsium and cæsium oxide) faces an anode rod in a vacuum bulb When light falls on the photo sensitive surface of the cathode electrons are emitted in linear proportion to the quantity of light falling If a current is passed through the bulb it is increased by the additional number of electrons emitted by the light-sensitive cathode The variations in current so produced are directly proportional to the amount of light received and can be recorded by means of a galvanometer with suitable valve amplification

The *photo conductive* cell depends on the increased electrical conductivity of certain semi conductors such as selenium when exposed to light The response is again linear The cell is made in the form of a selenium coated grid through which a current can be passed The electrical resistance of the cell varies inversely with the amount of light to which it is exposed and this variation can be recorded in the usual way

The *photo voltaic cell* depends on the fact that an electromotive force is generated when light falls on the interface between a layer of copper and a layer of copper oxide or between layers of iron and iron selenide The layer of cuprous oxide or iron selenide must be very thin (less than 0 01 mm) to allow the light to penetrate to the interface When the two layers are connected current flows in direct proportion to the quantity of light falling on the interface

ELECTROMANOMETERS transform pressures in the fluid system to equivalent electrical potentials directly and these are amplified sufficiently to operate suitable galvanometers A wide range of sensitivity allows pressure changes of 5 10 25 50 or 100 mm Hg to be represented by a deflection of 1 cm on the tracing *Transducers* for converting pressure changes into

equivalent variations in electrical potential are of various types according to the basic principle employed In practically all the fluid pressure acts on a membrane as with mechanical and optical manometers

The strain gauge makes use of the principle that wire increases its electrical resistance in proportion to the tension to which it is subjected Four strain sensitive wires are used and are attached to the membrane by cantilever suspension in such a way that movement in one direction increases the strain on one pair of wires and reduces it on the other movement in the reverse direction having the opposite effect When the membrane is at rest the resistances of the two pairs of wires are balanced on a Wheatstone bridge circuit When the resistances alter as a result of strain the bridge is thrown out of balance and current flows in the output or galvanometer circuit (Lambert and Wood 1947) If the bridge is powered by a 6 to 20 volt battery no amplification is necessary The frequency response is low at about 10 cycles per second The magnitude of the current is directly proportional to the movement of the membrane

Inductance transducers are based on Faraday s discovery in 1831 that an electrical current could be induced in a circuit by changing a magnetic field in the immediate vicinity of the circuit The induced current is increased if the coil is wound round a soft iron core If a battery current is flowing through the coil a magnetic field is set up around it which changes if the soft iron core is moved this change at once influences the current in the coil by setting up a secondary induced current Electromanometers have been designed in which the soft iron core of such a system is moved by a membrane influenced by changes of pressure (Wetterer 1944)

Condenser or capacitance manometers are based on the fact that if a condenser is incorporated in an alternating current circuit it acts like a resistance and since this resistance varies directly with the distance between the two plates the condenser can serve as a transducer if one of the plates is designed as a membrane which moves in response to changes of pressure Modern capacitance manometers are relatively complex (Hansen 1949)

Clinical arteriogram

Arteriograms are of limited clinical value because they reveal little that cannot be discerned with the trained finger A normal arteriogram (fig 5 01) usually exhibits two waves, P and D The former is the percussion wave and represents the rapidly transmitted shock of left ventricular contraction it is a pressure-wave and must not be confused with blood flow Its velocity is 5 to 8 metres per second and is inversely proportional to the elasticity of the artery The length of the wave is 3 5 to 5 metres The time lag between aortic and carotid events is about 0 03 second and between carotid and radial 0 10 second (Lewis 1925) The sharp upstroke of a brachial arteriogram usually measures about 0 08 second and the rounded summit of the tracing occupies a similar period D is the dicrotic wave and

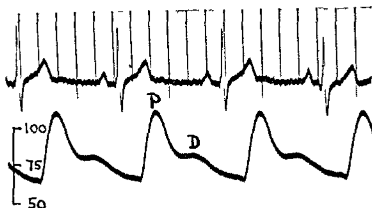


Fig 5 03—Normal arteriogram

is produced by the shock of aortic valve closure The latter synchronises with the *incisura (dicrotic or aortic notch)* which precedes the dicrotic wave Under certain circumstances e g in combined aortic stenosis and incompetence a second systolic wave T follows the percussion wave (fig 5 04)

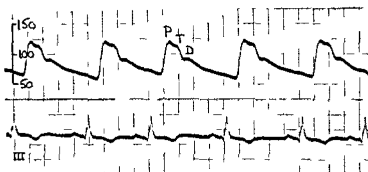


Fig 5 04—Direct arterial tracing showing a tidal wave T

Classical types of arteriogram have already been described in the clinical section on the pulse Direct arterial tracings are apt to be a little different and rather less like what one feels than the indirect The best example of this is the absence of a trough between percussion and tidal waves in the pulsus bisferiens in direct tracings (fig 2 04) The difference is attributed to the fact that a certain amount of external pressure is applied to the artery in indirect arteriograms just as it is when a clinician feels the pulse Direct tracings are similarly modified when external pressure is applied to the artery

The peak of the percussion wave of a direct arteriogram is the maximum systolic blood pressure the diastolic pressure is represented by the gentle

downward slope that succeeds the dicrotic wave The clinical diastolic pressure is the end of this slope i e the arterial pressure immediately preceding systole or the end diastolic pressure

A direct arteriogram may be recorded continuously over a long period if desirable e g when a continuous record of the blood pressure is required A special needle such as Riley s is then used and must be slipped well up the artery or a fine plastic catheter is threaded through the needle and the latter withdrawn Clotting may be prevented by including a slow high pressure saline drip in the system This does not influence the tracing

Arteriograms recorded simultaneously or consecutively with right ventricular pressures help to distinguish Fallot s tetralogy from pulmonary stenosis with normal aortic root in the former the systolic pressures are equal in the latter they are not The same principle serves to distinguish Eisenmenger s complex and pulmonary hypertension with reversed shunt through a patent ductus from other forms of pulmonary hypertension

Although the form of the arteriogram alone provides good evidence of the severity of aortic stenosis simultaneous brachial and left ventricular pressure tracings are better especially if the cardiac output at the time is known The left ventricular pressure is not easily measured but can be obtained by passing a fine nylon catheter through a needle inserted into the left atrium via the left bronchus or posterior chest wall (Bjork *et al* 1954) Direct puncture however is proving le s traumatic

Simultaneous or immediately consecutive direct arteriograms from the brachial and femoral arteries help to confirm or refute the presence of coarctation of the aorta when the diagnosis is in doubt In coarctation the femoral arteriogram shows a lower systolic pressure and a smaller pulse pressure than the brachial while the percussion wave is more prolonged and has a delayed summit

Continuous arteriograms have also proved helpful in the investigation of syncope and in studying the effects of the Valsalva manœuvre

The Valsalva manœuvre

The Valsalva manœuvre consists of forced expiration against a closed glottis (Valsalva 1707 Dawson 1943) It is a simple way of greatly raising the intrathoracic pressure The effect is more conveniently achieved by blowing up a column of mercury and maintaining the pressure at 50 mm Hg or as near to this level as possible This is then the intra oral pressure and may be assumed to be also the intrabronchial and intrapleural pressure Alternatively the intrathoracic pressure may be measured by passing a thin water filled polythene tube down the œsophagus (Dornhorst and Leathart 1952) the tube has an internal diameter of 0 5 mm and should have two or three lateral holes cut near the distal end The obstruction at the thoracic inlet tends to prevent cardiac filling and the heart

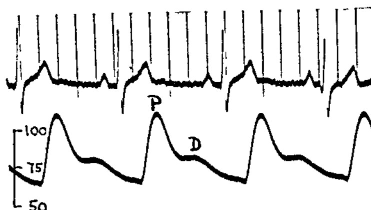


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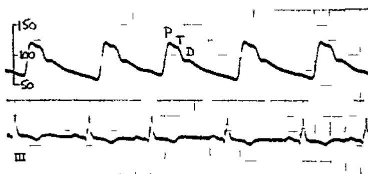


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THE CIRCULATION TIME

The circulation time may be measured from the antecubital fossa to the head and neck via the heart and lungs (Blumgart 1931) Numerous substances may be used for the purpose and fall chiefly into four groups illustrated by sodium cyanide histamine sodium dehydrocholate and fluorescein

If 0 25 to 0 5 ml of 2 per cent *sodium cyanide* is injected into the antecubital vein the patient takes a sudden deep breath when the substance reaches the carotid sinus the respiratory reflex being initiated by direct chemical action (Robb and Weiss 1934) At the same time the sinus node is depressed so that the objective end point is also signalled by a sinus pause which can be recorded and timed exactly on the electrocardiogram (Wexler *et al* 1947) Sodium cyanide is rapidly rendered inert by oxidation so that the test may be repeated almost immediately if necessary Unfortunately patients vary considerably in their susceptibility to the drug and as this cannot be predicted the minimum dose must be tried first the sensation of choking and strangling which may follow too large a dose in sensitive individuals may be very unpleasant *Lobeline* in doses of 2 5 to 5 mg acts similarly on carotid chemoreceptors and any record of respiration will signal the end point objectively It is safer and less unpleasant than cyanide (Berliner 1940)

Histamine phosphate (Weiss Robb and Blumgart 1928) in doses of 0 001 mg per kg of body weight in 1 5 000 solution induces a sudden facial flush when it reaches the capillaries of the head and neck It is not recommended owing to the uncertain end point and subsequent headache recorded times are too long

A 20 per cent solution of *sodium dehydrocholate* (decholin suprachol) has been used extensively and has given satisfactory results but sometimes causes vomiting (Winternitz *et al* 1931) A dose of 3 to 5 ml is injected rapidly through a wide bore needle the patient having been warned to raise the other hand smartly the instant he should notice a strange taste in or under the tongue This taste is peculiarly intense and bitter so that it is difficult for the patient to be mistaken about the moment of its arrival and objective confirmation may be obtained by the involuntary grimace that accompanies it The time should be measured from the beginning of the injection to the end point described A concentrated solution of *saccharin* (2 5 G in 4 ml of water) which produces a sweet taste when it reaches the tongue is less unpleasant does not cause vomiting and may be repeated if serial observations are required (Fishberg Hitzig and King 1933) but it is apt to cause local venous thrombosis *Calcium gluconate* 2 5 to 5 ml of a 20 per cent solution causes a hot sensation in the back of the tongue and throat (Goldberg 1936) and *magnesium sulphate* 6 ml of a 10 per cent aqueous solution has a similar end point (Neurath 1937 Bernstein and Simkins 1939) these substances may be alternated with advantage if test is repeated for they are physiological antidotes In this group

end points are all subjective but should not be despised on that account for they are usually sharp and clear.

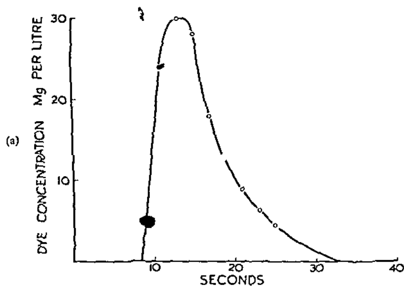
The fourth class comprises substances that give an objective end point wherever desired. In their original papers Blumgart and Weiss (1927) used *radium C* and a special detector which, operating at any given point in the circulation, would signal the arrival of the test dose. The same principle has been employed by Prinzmetal (1948) using *radiosodium* (Na^{24}) and a Geiger-Muller counter for constructing time concentration curves of the test dose as it passes through the right and left side of the heart. If within a minute of raising a histamine wheal (using 0.1 ml. of a mixture of equal parts of 1 : 1 000 histamine phosphate and 2 per cent procaine) on any part of the skin, a fluorescent substance is injected intravenously, fluorescence develops at the periphery of the wheal as soon as the substance reaches it; a suitable ultraviolet lamp is required. The best substances for this test are *fluorescein* (Lian and Barras 1930) and *riboflavine*, the dose of the former being 5.4 mg. per kilogram of body weight and of the latter 0.8 mg. per kilogram (Winsor *et al.* 1947).

The *normal arm to tongue circulation time* averages 13.5 seconds with extremes of 9 to 18 seconds (Wood 1936). *The time is fast* (6 to 9 sec.) in all the hyperkinetic circulatory states, and may be very fast (3 to 5 sec.) in congenital heart disease with large right to left shunt. *The time is greatly prolonged* in cases of left ventricular failure when it averages 28 seconds; it is variable in mitral stenosis according to the physiological situation, and only slightly prolonged, if at all, in pure right ventricular failure. The circulation time is also related to the size of the heart, particularly to the residual stroke volume (Gernandt and Nylin 1946), and is prolonged in myxœdema.

The *arm-to-lung time* may be measured by injecting 0.25 ml. of ether into the antecubital vein, its arrival in the capillaries of the lung being signalled by a sudden cough or deep breath and by the smell of ether in the expired air. Amyl acetate may also be used, the smell of pear drops being unmistakable when it reaches the lungs. The normal time averages 6 seconds and ranges between 3.5 and 8 seconds (Hitzig 1935). The test has limited value as explained on page 278.

DYE DILUTION CURVES

The injection method of measuring the cardiac output (Stewart 1897) was taken up in 1929 by Kinsman, Moore and Hamilton who studied the behaviour of a small quantity of dye when injected rapidly into models of the circulation. The dye diffused uniformly in the turbulent stream and moved forwards in an ever widening band. If samples of the fluid stream were taken at frequent intervals from a point well away from the site of injection and the quantity of dye in each sample measured colorimetrically against known standards, a curve could be constructed in which the concentration of dye in mg. per litre was plotted against the time (in



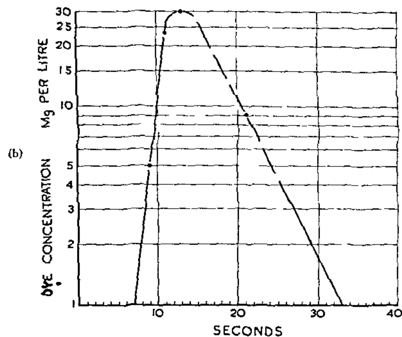


Fig 5 06—Time concentration curves
(a) Plotted in a l near manner on both s ales
(b) Concentration plotted logarithmically (see text)

seconds) at which the sample was obtained after the onset of the injection Such time concentration curves had a characteristic shape as shown in figure 5 06a. The build up of concentration second by second was rapid the disappearance of dye more gradual and fading off towards infinity If recirculation was arranged to make the model more realistic the downstroke of the curve was interrupted by a sudden increase of concentration as the dye entered its second circuit This made it impossible to estimate the time at which the dye would have disappeared from samples had it not recirculated The difficulty was overcome when it was recognised that the down stroke of the curve had a logarithmic shape and when the concentration of dye was plotted logarithmically the time scale remaining linear the downstroke became a straight line (fig 5 06b) By extending the top part of the slope until it met the time scale it was then possible to tell when the dye would have disappeared had it not recirculated

Suppose now the duration of such a time concentration curve is 30 seconds and the mean concentration of dye over that period is 10 mg per litre then if the amount of dye injected was 20 mg it is clear that this must have been diluted by 2 litres of blood in 30 seconds i e by a blood flow or cardiac output of 4 litres per minute

$$\text{Thus F or C O} = \frac{1 \times 60}{ct}$$

where F is the blood flow in litres per minute
- i is the quantity of dye injected in mg
- c is the mean concentration of dye in mg per litre
- t is the duration of the time concentration curve in seconds

The mean concentration of dye is the average of all the samples taken second by second over the period of the time concentration curve In the hypothetical curve plotted in fig 5 06 the mean concentration of dye works out at 12 mg per litre over a period of 24 seconds Had 24 mg of dye been injected the cardiac output per minute would have been $\frac{24 \times 60}{12 \times 24} = 5$ litres

When compared with the Fick principle for measuring cardiac output in animals results obtained by the dye injection method tallied remarkably closely the average difference between the two being only 0 2 per cent (Moore *et al* 1929) Nearly twenty years later Hamilton and his colleagues (1948) compared the two methods in man and again average results were almost identical

The dye commonly used now is Evans blue in a dose of 10 to 20 mg (2 to 4 ml of a 0 5 per cent solution) An ear oximeter of the photo electric cell type designed by Millikan (1942) and modified by Wood and Geraci (1949) may be used instead of direct arterial sampling at two second intervals Time concentration curves can be recorded directly by means of a galvanometer with this oximeter (Beard and Wood 1951)

Dye dilution curves may also be used in the study of intracardiac shunts

and other cardiovascular abnormalities (Nicholson Burchell and Wood 1951) With left to right shunts as in atrial septal defect ventricular septal defect and patent ductus the initial part of the curve is more or less normal in that dye arrives at the ear in normal time builds up quickly and starts disappearing quickly although its mean concentration is diminished but recirculation occurs early and may be repeated once or twice producing a series of irregular bumps during the return of the graph to normal With right to left shunts as in Fallot s tetralogy dye arrives at the ear well ahead of normal time giving rise to a premature hump on the upstroke of the normal curve (Swan *et al*, 1953)

Pulmonary blood volume

Dye dilution curves offer an objective method of measuring the mean pulmonary circulation time (Hamilton *et al* 1932), and since the cardiac output at the time can be estimated by the same technique the amount of blood in the lungs can be calculated from Stewart s formula which states that

$$Q = \frac{VT}{60} \text{ (Stewart 1921)}$$

where Q is the quantity of blood in the lungs in litres
V is the pulmonary blood flow in litres per minute and
T is the mean pulmonary circulation time in seconds

In the hypothetical example illustrated in figure 5 06

$$Q = \frac{5 \times 12 \text{ (say)}}{60} = 1 \text{ litre}$$

When measuring the pulmonary circulation time by means of radium C Blumgart and Weiss (1928) calculated that the average quantity of blood in the lungs of normal subjects was 984 ml or 21 per cent of the total blood volume

Total blood volume

The circulating blood volume is normally around 5 to 6 litres it is about 3 to 3 5 litres per square metre of body surface or about 75 to 85 ml per kilogram of body weight and averages a little more in men than in women owing to a rather higher red cell content in men Plasma constitutes about 55 per cent and cells about 45 per cent of the volume of whole blood

It may be estimated by injecting intravenously a known quantity of a substance with suitable characteristics and measuring its concentration in the blood after complete mixing has occurred Evans blue dye (Gregersen *et al* 1935) has proved satisfactory and may be given in a dose of 5 ml of a 0 5 per cent solution its concentration in the plasma being determined colorimetrically The dye technique originally introduced by Keith Rowntree and Geraghty in 1915 has largely replaced the older carbon monoxide method of Haldane and Smith (1900) in which a known quant

of the gas was inhaled and its concentration in the blood measured by means of a colorimeter or by blood gas analysis The injection of radio active substances such as tagged red cells is now challenging the dye method or is being employed as a supplement to it for tagged red cells are used for measuring the total circulating red cell volume whereas dyes measure plasma volume Of course the relative quantities of red cells and plasma in whole blood can be determined easily by the hæmatocrit

CARDIAC CATHETERISATION

Although first performed by Forssmann (1929) on himself the introduction of cardiac catheterisation as an aid to clinical diagnosis is largely due to the work of Cournand (1941) in the U S A and of McMichael and Sharpey Schafer (1944) in England

Cardiac output

Up till then measurement of cardiac output in man depended on methods which could not directly utilise the important principle first enunciated by Fick (1870)

$$\text{C O (L /min)} = \frac{\text{oxygen consumption (ml min)}}{\text{A}-\text{V oxygen difference (ml /L)}}$$

For example, if an individual extracts 250 ml of oxygen from the atmos phere per minute and the difference in oxygen content between samples of blood from the pulmonary artery and samples from the pulmonary veins (arterio venous oxygen difference) is 50 ml per litre then clearly 5 litres of blood must have passed through the lungs per minute It was easy enough to measure the oxygen consumption and the oxygen content of arterial samples but short of direct puncture there was no means of obtain ing a mixed venous sample from the right side of the heart Cardiac catheterisation however at once made this possible and since its intro duction a vast amount of accurate work on the cardiac output in health and disease has been carried out

Pressures in the lesser circulation

At the same time cardiac catheterisation supplied another great need for it offered a direct and relatively safe method of measuring *pressures in the right side of the heart* and pulmonary artery—a previously inaccessible part of the circulation Hamilton s optical manometer already in use for measuring arterial pressure (q v) allowed systolic and diastolic pressure to be measured accurately and soon a number of electromanometers were adapted or designed for the same purpose

It was discovered later that if the catheter was passed down a branch of the pulmonary artery as far as it would go the tip usually became wedged in such a manner that a little force was required to withdraw it The pressure recorded when the catheter was so wedged was called the *pul monary capillary venous pressure* for it was believed to represent just that

(Hellems *et al* 1948 Lagerlof and Werko 1949) Samples withdrawn from such a site are always near 100 per cent oxygenated and must not be used as an indication of the oxygen saturation of pulmonary venous blood In fact however the pressure obtained when a catheter is wedged in a pulmonary artery branch is the left atrial pressure (fig 5 07) and the wave

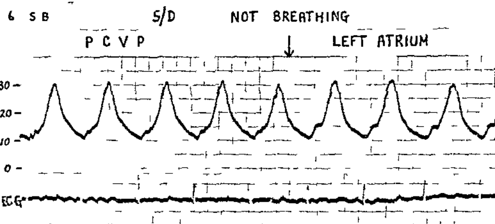


Fig 5 07—Immediately consecutive tracings from a wedged pulmonary artery and from the left atrium (via the left bronchus) in a case of mitral incompetence showing an identical pressure pulse in the two situations (from the paper by Epps and Adler from the Cardiac Department of the Brompton Hospital)

form is identical with the left atrial pressure pulse (Epps and Adler 1953)

If the left atrial pressure pulse cannot be obtained indirectly in this way it can be recorded directly by inserting a needle into the left atrium via the left bronchus (Facquet Lemoin *et al* 195-) or by paravertebral puncture (Bjork *et al* 1953) Even left ventricular pressures can be recorded via similar routes (Bjork *et al* 1954)

The pulmonary vascular resistance can be calculated when the cardiac output mean pulmonary artery pressure and mean left atrial pressure are known according to Poiseuille s equation

$$\text{Resistance (R)} = \frac{\text{pressure gradient}}{\text{flow}}$$

which adapted becomes

$$R = \frac{\text{P A P} - \text{L A P (mm Hg)}}{\text{pulmonary blood flow (L / min)}}$$

The result may be expressed in simple units of resistance If it is desired to express resistance in fundamental units of force as described by Gorlin and Gorlin (1951) pressures in mm Hg must be converted into

dynes/cm and flows expressed in litres per minute must be converted in cm ^{3}/sec The equation thus becomes

$$R = U \times \frac{0\ 1 \times 13\ 59 \times 981\ 17\ \text{dynes/cm}}{1\ 000\ \text{cm}^3/60\ \text{sec}}$$

where U stands for the simple unit already described The figure 13 59 is the specific gravity of mercury and 981 17 cm per second per second is the g factor—that is the acceleration force of gravity The dividend thus becomes 1 333 4 dynes/cm The equation may now be rewritten

$$R = U \times \frac{1\ 333\ 4\ \text{dynes} \times 60\ \text{sec}}{1\ 000\ \text{cm}^5}$$

$$= U \times 80\ 004\ \text{dynes sec /cm}^5$$

Thus it is only necessary to multiply the unit by 80 to express the resistance in dynes sec /cm ^{5}

Shunts

As cardiac surgery advanced accurate methods of diagnosing the various forms of congenital heart disease became imperative and in this new field cardiac catheterisation helped enormously In left to right shunts samples from chambers beyond and including that which receives the shunt contain more oxygen than samples taken from chambers proximal to the shunt For example in ventricular septal defect samples from the venæ cavæ and right atrium may be 70 per cent saturated with oxygen when samples from the right ventricle and pulmonary artery are 80 per cent saturated proving that arterialised blood has entered the right ventricle from the left side of the heart Since the pulmonary blood flow and the systemic blood flow can be measured separately, the size of the shunt can be calculated

$$\underset{(\text{L /min})}{\text{Pulmonary flow}} = \frac{\text{oxygen consumption (ml /min)}}{\text{P V} - \text{P A oxygen content (ml /L)}}$$

$$= (\text{say}) \frac{240}{190 - 160} = 8\ \text{L /min}$$

$$\underset{(\text{L /min})}{\text{Systemic flow}} = \frac{\text{oxygen consumption (ml /min)}}{\text{Art} - \text{R A oxygen content (ml /L)}}$$

$$= \frac{240}{190 - 140} = 4\ 8\ \text{L /min}$$

Thus in this example the interventricular shunt is 3 2 L /min Pulmonary venous blood can only be obtained if the catheter passes through a foramen ovale but for practical purposes may be assumed to be the same as arterial blood provided there is no right to left shunt

In cases of right to left shunt samples from all chambers in the right side

of the heart are similar but the arterial oxygen saturation is reduced In such cases

$$\text{Pulmonary flow} = \frac{\text{oxygen consumption}}{\text{P V} - \text{P A oxygen content}}$$

$$= (\text{say}) \frac{210}{190-120} = 3\ \text{I /min}$$

$$\text{Systemic flow} = \frac{\text{oxygen consumption}}{\text{arterial} - \text{R A oxygen content}}$$

$$= (\text{say}) \frac{210}{160-120} = 5\ 2\ \text{L /min}$$

giving in this instance a right to left shunt of 2 2 L /min In making the calculation it has been assumed that the pulmonary venous blood is 95 per cent saturated i e having an oxygen content of 190 ml /L (oxygen capacity with normal hæmoglobin 200 ml /L) It should perhaps be explained that in calculating the systemic blood flow the arterial oxygen content from which the arterio venous oxygen difference is partly derived is made up of two components the content of blood which has passed through the lungs and picked up all the oxygen consumed and the content of the shunted blood which has picked up no oxygen at all It is as if the full 5 2 litres passed through the lungs but 2 2 of them failed to pick up any oxygen

Further information in congenital heart disease may be obtained if the catheter passes through a septal defect into the left side of the heart or into anomalous veins

TECHNIQUE

Radio opaque nylon catheters 100 to 125 cm long are made in seven sizes (nos 4 to 10) the smallest (no 4) having an internal diameter of 0 5 mm and an external diameter of about 1 3 mm and the largest (no 10) having an internal diameter of about 1 8 mm and an external diameter of 3 2 mm when filled they contain from 0 3 to 3 9 ml of saline the common sizes (nos 6 7 and 8) containing 0 8 1 2 and 1 5 ml respectively They are sufficiently pliable to loop easily inside the heart or blood vessels yet not so soft as to lose their elasticity as soon as they are warmed in the blood stream The distal end is bent at about 4 cm from the tip so that awkward angles can be negotiated After use the catheters are washed out with tap water and then with a hydrogen peroxide drip for several hours to remove any particles of blood enmeshed in the weave with which the catheters are lined if this is neglected rigors may arise from pyrogens washed out of the lining of the catheter when it is next used and can be very dangerous in certain types of heart disease The catheters are then sterilised in hot formalin vapour and may also be stored in formalin vapour They should not be boiled or autoclaved

The patient is prepared with omnopon gr 1/6 to 1/4 or pethidine 50 to 100 mg and phenergan 25 mg The latter acts as an additional sedative and tends to prevent vomiting Pentothal may be necessary in children under six Neither quinidine nor procaine amide are now given as a routine beforehand because they did not prevent or diminish the frequency of ectopic beats or other changes of rhythm and they are undesirable for three other reasons (1) they may diminish the peripheral resistance (2) they encourage cardiac standstill in the rare event of transient heart block during catheterisation (3) they may turn pre existing or a paroxysm of atrial fibrillation into flutter with a faster ventricular rate Procaine amide, however is always kept handy so that 0 5 to 1 G may be given through the catheter immediately in the event of paroxysmal ventricular tachycardia or fibrillation Noradrenalin 100 μg in 10 ml of sterile water is also kept ready in a second syringe in hazardous cases for restoration of normal rhythm by means of heavy doses of procaine amide may not restore the blood pressure Penicillin, 1 million units is given as a routine to help prevent infection

The patient is laid flat on a foam rubber mattress overlying an X ray couch a window is cut out of the mattress to facilitate fluoroscopy The couch should be constructed so that it can be tilted easily and should be freely accessible from either side

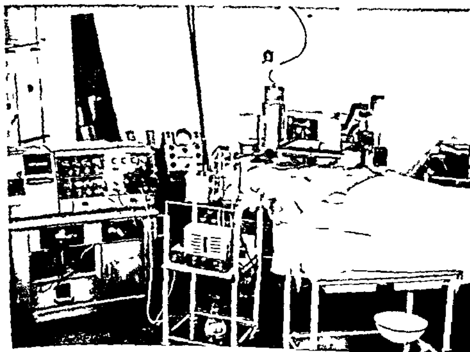


Fig 5 08—Photograph of the N E P multichannelled recorder Sanborn *electromanometer* and cathode ray monitor used for cardiac catheterisation at the Institute of Cardiology

The right median cubital vein or the right basilic vein below or above its junction with the cubital vein is exposed after liberal dermal anaesthesia with 1 per cent procaine *The right arm is preferred because* the catheter is easier to manipulate from this side (especially if the operator is right handed) because the route is a little shorter (important in large adults if an indirect left atrial pressure tracing is required) and to avoid a left sided superior vena cava entering the right atrium via the coronary sinus a very difficult route from which to catheterise the pulmonary artery (encountered in 6 per cent of cases especially in Fallot s tetralogy) *The median vein* is always chosen because it offers no obstruction to the passage of a catheter whereas the cephalic route proved impossible in 19 out of 30 cases in which it was tried *Liberal dermal anæsthesia* means raising an extensive wheal in the skin overlying the vein using about 10 ml of 1 per cent procaine subcutaneous anæsthesia wears off too quickly and stronger solutions of procaine are initially more painful and may upset previously good sedation in a small child Efficient dermal anæsthesia has made venospasm very rare

A catheter should be chosen which fits the vein snugly if too large it will be difficult to move freely and will excite venospasm if too small bleeding will be troublesome As a rule size 8 is best for adults with good veins no 7 for children and adults with small veins and no 6 for smaller children The larger the catheter the easier it is to see a point of some importance when the heart is large A no 6 catheter is also advised for cases of severe pulmonary stenosis with normal aortic root when there is some danger of a large catheter blocking the pulmonary outflow

When all is ready the vein is opened and the catheter which has been previously washed inside and out with saline to remove all traces of formalin and to the hilt of which is attached a 5 or 10 ml syringe loaded with saline is inserted in the manner of introducing a cannula and pushed up the vein its curved tip being directed medially and care being taken to avoid introducing air Any obstruction can usually be overcome by rotating the catheter a little one way or the other When the tip is judged to be in the neighbourhood of the superior vena cava the lights are turned out 5,000 units of heparin are given through the catheter and the inelastic sterile tube which will connect the catheter with the electromanometer is set up ready for use while the operator is accommodating the rest of the procedure being under fluoroscopic control Kinks at the thoracic inlet may be passed during deep inspiration abducting the arm or altering the position of the head and neck are usually a waste of time If the obstruction appears insuperable it can be overcome by allowing the tip of the catheter to enter the jugular and to rotate it this way or that until some resistance is felt if then the catheter is pushed gently forwards a loop will form near the tip and this is encouraged until the bend itself passes down the superior vena cava In over 1 000 pulmonary artery catheterisations the right superior vena cava has never be[illegible]sent and if there was no clini

The patient is prepared with omnopon gr 1 6 to 1 4 or pethidine 50 to 100 mg and phenergan 25 mg The latter acts as an additional sedative and tends to prevent vomiting Pentothal may be necessary in children under six Neither quinidine nor procaine amide are now given as a routine beforehand because they did not prevent or diminish the frequency of ectopic beats or other changes of rhythm and they are undesirable for three other reasons (1) they may diminish the peripheral resistance (2) they encourage cardiac standstill in the rare event of transient heart block during catheterisation (3) they may turn pre existing or a paroxysm of atrial fibrillation into flutter with a faster ventricular rate Procaine amide, however, is always kept handy so that 0 5 to 1 G may be given through the catheter immediately in the event of paroxysmal ventricular tachycardia or fibrillation Noradrenalin 100 μg in 10 ml of sterile water is also kept ready in a second syringe in hazardous cases for restoration of normal rhythm by means of heavy doses of procaine amide may not restore the blood pressure Penicillin, 1 million units, is given as a routine to help prevent infection

The patient is laid flat on a foam rubber mattress overlying an X ray couch a window is cut out of the mattress to facilitate fluoroscopy The couch should be constructed so that it can be tilted easily and should be freely accessible from either side

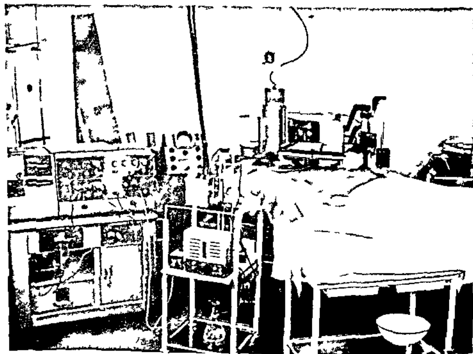


Fig 5 08—Photograph of the N E P multichannelled recorder Sanborn electromanometer and cathode ray monitor used for cardiac catheterisation at the Institute of Cardiology





(a) Anterior view
(b) First oblique position
(c) Second oblique position

Fig 5 10—Catheter in right pulmonary artery




(a) Anterior view
(b) First oblique position

Fig 5 11—Catheter in the left pulmonary artery



Fig 5 11(c)—Catheter in left branch of the pulmonary artery (nd oblique position)



Fig 5 12—Showing a catheter in the left upper pulmonary vein after passing through a foramen ovale in a normal subject

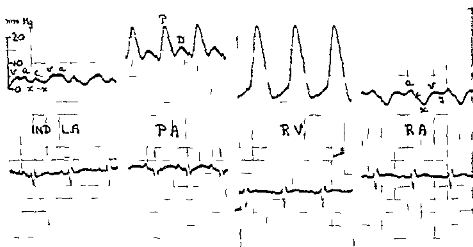


Fig 5 13—Normal pressure pulses from the left atrium (indirect) pulmonary artery right ventricle and right atrium

evidence of thrombosis the vessel has never been blocked With the aid of deep inspiration and this easily formed loop difficulty in entering the superior vena cava has been overcome in all cases

As soon as the catheter lies in the right atrium its hilt should be connected to the electromanometer and the right atrial pressure pulse recorded simultaneously with the electrocardiogram The variable hydraulic damper is then adjusted and the recording system tested while the operator accommodates more thoroughly Direct writing multichannel recorders have proved very satisfactory for routine diagnostic work if a photographic recording system is used it is imperative to have a cathode ray monitor as well so that tracings can be inspected continually The zero reference point to which the manometer is adjusted may be the sternal angle or a measured distance such as 10 cm above the surface of the couch which represents the expected level of the heart itself There is some advantage in incorporating a high pressure very slow heparinised saline drip in the hydraulic system to combat any possibility of clotting in the lumen of the catheter but with due care thrombosis can be avoided without it Blood should never be allowed to enter the catheter inadvertently and when deliberately withdrawn (as in sampling) or when assumed to have entered (as when advancing into a high pressure zone with the hilt of the catheter attached to an unattended syringe) it should be cleared as soon as possible by injecting saline from the syringe This is not only to avoid clotting but also to prevent particles of blood becoming enmeshed in the weave with which the catheter is lined—a fruitful source of future pyrogens and rigors

The best way to enter the right ventricle from the right arm is to allow the tip of the catheter to impinge against the lateral wall of the right atrium and by pushing on to form a loop there when rotated medially this loop ensures that the tip of the catheter is directed upwards when it passes through the tricuspid valve and so passes on readily into the pulmonary artery (fig 5 09) The position of the catheter is determined by fluoroscopy by the pressure pulse recorded and if necessary by sampling For example if the tip of the catheter looks as if it were in the outflow tract of the right ventricle but will not pass onwards the pressure pulse will probably be atrial in form and a blood sample may be bright red from the left atrial appendix or almost black from the coronary sinus

Typical positions are illustrated in figures 5 10 to 5 12 and a normal series of pressure pulses in figure 5 13 As previously mentioned an indirect left atrial pressure pulse may be obtained by wedging the tip of the catheter in a distal branch of the pulmonary artery so that a little force is required to withdraw it If the catheter can be passed through a patent foramen ovale or atrial septal defect an indirect pulmonary artery pressure tracing may also be recorded by wedging the catheter in a pulmonary vein (fig 5 14)

Samples of blood (5 ml) are withdrawn under paraffin from all important positions which the catheter has entered preferably in quick

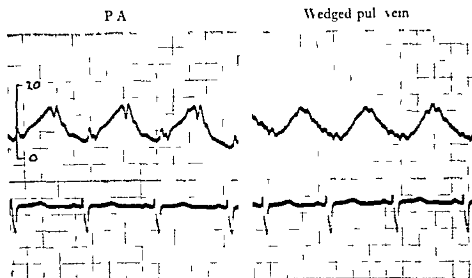


Fig 5 14—Pulmonary artery pressure pulse recorded indirectly by wedging a catheter in a pulmonary vein

and an arterial sample is obtained simultaneously with that from the pulmonary artery The samples are expelled from the syringe by means of a long needle or cannula into the bottom of small glass vessels containing a bead of heparin under a layer of liquid paraffin In both the syringe and container the paraffin keeps the samples free from contact with air They *should be analysed for oxygen content or unsaturation by means of Van* Slyke s or Haldane s method respectively as soon as possible if blood gas analysis is delayed for several hours the samples should be stored in a refrigerator

The *total screening time* should not exceed 30 minutes at 1 m a

On withdrawing the catheter the vein is usually ligated attempts to save its lumen by passing skin sutures under the vein above and below the opening in its wall have been none too successful and occasionally appreciable hæmorrhage has occurred

Complications

Venospasm often proved troublesome in the early days it has been *practically abolished by efficient local anæsthesia and by selecting a catheter* that is not too large for the vein Its present 2 per cent incidence seems to be associated with inadequate sedation in unduly nervous individuals or improper washing of the catheter so that traces of formalin still remain on its surface

Ectopic beats are extremely common and may be disregarded They occur especially when the tip of the catheter lies in the body of the right ventricle

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA, usually 2–1 auricular flutter occurred in 3 3 per cent of 1 000 cases catheterised at the National Heart Hospital or Brompton Hospital It occurred in 11 4 per cent of 88 cases of atrial septal defect in 9 per cent of 45 cases of ventricular septal defect but not more frequently than in normal subjects (4 per cent of 50 cases) in any other condition For example it occurred in 2 4 per cent of 335 cases of mitral valve disease and in 2 per cent of 145 cases of pul monary stenosis with normal aortic root It did not occur at all in 60 cases of patent ductus in 75 cases of Fallot s tetralogy nor in 48 cases of pulmonary hypertension with reversed shunt

PAROXYSMAL VENTRICULAR TACHYCARDIA is fortunately rare (1 per cent) although short bursts of ventricular ectopics are common enough

VENTRICULAR FIBRILLATION occurred in three cases once in Ebstein s disease once in advanced atrial-septal defect and once in primary pul monary hypertension it resulted in immediate death in two of them giving a mortality rate of 0 2 per cent for the whole series

TRANSIENT RIGHT BUNDLE BRANCH BLOCK occurred in 5 per cent In one such instance in which permanent left bundle branch block was already present this resulted in 2–1 heart block and might well have been serious Since then left bundle branch block has been considered a contraindication to catheterisation

TRANSIENT NODAL RHYTHM developed in 1 5 per cent and was in consequential

AIR EMBOLISM could occur if the operator was careless and might have dire consequences in cases with right to left shunt None was recognised in this series however but particular care has always been taken to keep the hilt of the catheter below right atrial level when sampling

THROMBO EMBOLISM was also totally avoided although clotting in the catheter occurred in 1 per cent This was nearly always the fault of the operator and should have been prevented Subsequent phlebothrombosis was not uncommon but pulmonary embolism was very rare (0 05 per cent) and never serious Such cases however were treated with heparin and dindevan

CEREBRAL ABSCESS which may have been due to paradoxical embolism occurred in two cases of Fallot s tetralogy one just before catheterisation was about to be undertaken the other a month afterwards

RIGORS due to pyrogens washed out of improperly cleaned catheters in which blood had been allowed to lie too long on a previous occasion were very troublesome indeed before the catheters were treated with a hydrogen peroxide drip after use There have been only two in the last 500 cases

SYNCOPE due to blocking the outflow tract of the right ventricle with the catheter at valve or infundibular level occurred in three cases of severe pulmonary stenosis with normal aortic root two with reversed interatrial shunt an incidence of about 6 per cent but in no other condition Vaso motor syncope associated with anxiety occurred twice in the series

WOUND SEPSIS has never been serious but can be a nuisance to both patient and staff its frequency is naturally inversely related to the amount of care and trouble spent on proper aseptic precautions

Contra indications

1 Cases of known *ischæmic heart disease* should not be catheterised at all under any circumstances Three instances are known to the author one died immediately from ventricular fibrillation the other two both developed paroxysmal ventricular tachycardia and the procedure was abandoned

2 *Ebstein s disease* is dangerous Out of six I have personally catheterised one died immediately from ventricular fibrillation and one developed paroxysmal tachycardia which could have been ventricular I know of two other deaths amongst the relatively few cases of Ebstein s disease in the world that have been catheterised

3 Cases with *left bundle branch block* run a 5 per cent risk of developing transient bilateral branch block which could well result in complete heart block

4 Cases of *advanced atrial septal defect* with gross dilatation of the right side of the heart need very careful handling one of the two deaths in the series here analysed occurred in such a case and another is known to the author

5 Advanced *anoxic cor pulmonale* has been responsible for at least one death from cardiac catheterisation

In a review of 973 catheterised cases Hebert Scebat and Lenegre found the mortality was 0 7 per cent Two of the deaths were due to cardiac hæmorrhage from trauma two to severe rigors one to acute pulmonary œdema and three to subsequent pulmonary embolism *Acute pulmonary œdema* occurred in 14 of their series cases of mitral stenosis in which the pulmonary vascular resistance is judged to be low should be treated with great respect preliminary dehydration is important and the X ray couch should be tiltable foot down

A mortality rate of 0 2 per cent in 1 000 cases was reported by Zimdahl (1951) and of 0 1 per cent in 5 691 cases by Cournand *et al* (1953)

Normal pressures

There were 50 normal subjects amongst the *1 000 catheterised* The figures given here are based on these The reference point to which the pressures are related is the sternal angle so that they are all 3 to 5 mm Hg lower than those generally reported

The right atrial pressure averaged −0 5 −4 −1 5 −1 mm Hg for *a x v* and *y* respectively the average mean pressure being −1 3 mm Hg with reference to the sternal angle The range of the mean pressure was +2 to −5 The significance of *a x v* and *y* has already been discussed (p 47)

The indirect left atrial pressure averaged 4 mm Hg higher with little to choose between *a* and *v* or *ac* and *v* in good tracings sound artifacts made

precise measurements difficult at these low pressures

The right ventricular pressure averaged 16/—1 with a mean of 4 mm Hg The highest systolic pressure recorded was 25 mm Hg very few being over 20 and only one under 10

The pulmonary artery pressure averaged 16/7 mm Hg and the mean 11

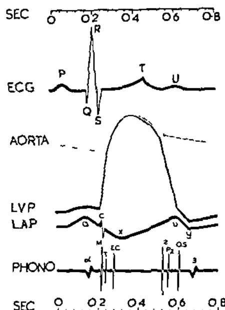


Fig 5 15—Time relationships between electrocardiogram aortic left ventricular and left atrial pressure pulses and the phonocardiogram (see text)

Time relationships of central pressure pulses (fig 5 15)

The first recordable event in the cardiac cycle is the right atrial or first half of the P wave of the electrocardiogram The *a* wave of the right atrial pressure pulse begins at the peak of P and reaches the jugular pulse about 0 1 second later

The *x* descent due to atrial relaxation begins before ventricular systole and is interrupted by a notch or deformity representing closure of the tricuspid valve this is the right atrial *c* wave It is rarely large enough to be seen in the jugular pulse

The left atrial *c* wave is synchronous with the onset of left ventricular systole with the mitral element of the first heart sound and with the S wave of the electrocardiogram The right atrial *c* wave probably occurs 0 02 to 0 03 second later and is synchronous with the onset of right ventricular systole and with the tricuspid component of the first sound

The *x* descent of the right atrial pressure pulse continues after the *c* interruption the systolic part of the trough being partly attributed to descent of the base the atrio ventricular septum moving downwards and to the left towards the apex of the heart as the ventricles contract so creating negative pressures in the atria

Isometric ventricular contraction is that part of ventricular systole that occupies the time interval between closure of the tricuspid and mitral valves and the opening of the pulmonary and aortic valves respectively a matter of 0 04 to 0 05 second

The opening of the semi lunar valves which signals the end of the isometric contraction phase occurs about 0 03 second before the vascular components of the first heart sound These are normally inaudible but under certain circumstances they can be heard as systolic ejection clicks

Thus the time interval between the mitral component of the first heart sound and an aortic ejection click is a measure of the duration of left ventricular isometric contraction if 0 03 second delay is allowed (Leatham 1954)

The ejection phase then begins and lasts about 0 25 second two thirds of the ventricular stroke volume are pumped into the great vessels during the first half of this period (Wiggers 1921) The carotid pulse and the carotid *c* wave of the jugular phlebogram follow left ventricular ejection by about 0 03 second and the radial pulse is some 0 10 second later (Lewis 1925)

Protodiastole is the short period of ventricular relaxation between the end of the ejection phase and closure of the semilunar valves The aortic valve normally closes before the pulmonary and synchronises with the first component of the second heart sound and more or less with the end of the T wave of the electrocardiogram

The isometric relaxation phase is the time occupied by the ventricles between closure of the semilunar valves and the opening of the atrio ventricular valves (0 06 to 0 10 sec) The two components of the second heart sound signal its onset in respect of each ventricle (P falling 0 02 to 0 05 second after A) and the top of the *v* waves of right and left atrial pressure tracings signal its end in respect of each ventricle The opening snap of mitral stenosis also synchronises with the end of left ventricular isometric relaxation in that disease

After the opening of the mitral and tricuspid valves atrial and ventricular diastolic pressures fall together this is the *y* descent or downstroke of *v* seen in atrial pressure pulses The subsequent rise of diastolic pressure in both atria and ventricles depends on the venous pressure gradient and the tone of the ventricles As used here ventricular tone may be defined as resistance to diastolic filling Since the left atrial pressure averages 4 mm Hg higher than the right it must be assumed that the left ventricular diastolic pressure is also 4 mm Hg higher than the right and this may be a function of tone

From these time relationships it may be observed that if the heart rate is 60 beats per minute allowing 1 second for the length of each cycle the ventricles are allotted 0 62 second in which to fill and 0 28 second in which to contract, 0 10 second being expended in protodiastolic and isometric relaxation

Normal samples

The oxygen capacity is the total amount of oxygen held by a litre of blood when fully saturated Since 1 G of hæmoglobin will hold 1 34 ml of oxygen at normal temperature and pressure a litre of normal blood will hold 15×1 34×10 = 201 ml of oxygen when fully saturated

The arterial oxygen saturation is normally 95 per cent of its oxygen capacity. This means that a litre of normal arterial blood holds $\frac{95}{100}$ of 201 = 191 ml of oxygen.

Samples of arterial blood may be obtained from the brachial or femoral artery by direct puncture. A sharp short bevelled 18 gauge needle attached to an all glass syringe containing a little paraffin should be plunged into the vessel. The arterial blood pressure then lifts the barrel of the syringe spontaneously, little aspiration being necessary. On withdrawing the needle the site of puncture should be compressed digitally for at least a minute.

The oxygen content of a sample is the actual amount of oxygen it contains and may be measured by means of Van Slyke's apparatus. Thus the oxygen content of normal arterial blood in the example given above is 191 ml per litre. This is sometimes expressed as 19.1 volumes per cent.

The oxygen unsaturation of a sample is its oxygen capacity less its oxygen content, and may be measured by means of Haldane's apparatus. Thus the normal arterial oxygen unsaturation is around 10 ml per litre or 1 volume per cent.

The arterio venous oxygen difference averaged 34 ml per litre in our series of 50 normal subjects, the range being 21 to 48.

The cardiac output calculated from Fick's formula (q.v.) averaged 8.6 litres per minute, the range being 5.8 to 12.8. These figures are not basal, but they certainly represent what is actually found under the conditions inevitably associated with cardiac catheterisation. The *basal cardiac output* is said to be around 4 to 5 litres per minute and is about a litre higher in the horizontal than in the erect position (McMichael and Sharpey Schafer, 1944). The *cardiac index* is the cardiac minute output per square metre of body surface and should be around 3.

Samples from the right side of the heart (superior vena cava, right atrium, right ventricle and pulmonary artery) should not differ by more than 5 per cent in oxygen saturation, the scatter being centred around a mean difference of 3 per cent in our series. The *average oxygen saturation* of all these samples was 75 per cent, the vast majority being between 70 and 80 per cent.

The *pulmonary vascular resistance* (q.v.) averaged 1 unit or 80 dynes sec/cm[5], commonly ranging between 0.5 and 1.5 units. The maximum normal resistance was 2.5 units.

OXIMETRY

Photovoltaic iron selenium ear oximeter are based on the principle that oxyhæmoglobin and reduced hæmoglobin absorb light differently. Two cells are used. One is covered by a green Wratten 61 N filter which responds to light with wave lengths of 480 to 600 millimicrons and 750 to 800 millimicrons, the intermediate part of the spectrum being filtered out. Both oxy and reduced hæmoglobin transmit light of these wave lengths equally

so that the output of this cell depends on the thickness of the ear and the amount of blood in it The second cell is covered by a red Wratten 29 F filter which transmits light with wave lengths of 600 millimicrons and above Since this red portion of the spectrum is absorbed in much greater degree by reduced hæmoglobin than oxyhæmoglobin the amount of light activating this cell is proportional to the percentage of oxyhæmoglobin present in the blood through which the light passes the first cell balancing the second in respect of other variables (Millikan 1942)

RESPIRATORY FUNCTION TESTS

An elementary knowledge of respiratory physiology is essential to a proper understanding of the circulation

CHEMICAL AND NERVOUS CONTROL OF BREATHING

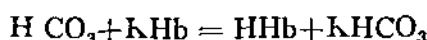
When discussing the causes of dyspnœa it was observed that the respiratory centre reacted to several independent stimuli and that the total response depended on the algebraic sum of these stimuli (Gray 1950)

ANOXIA (as diminished oxygen tension in the plasma) is a relatively weak stimulus which acts on chemoreceptors in the carotid sinus and aortic bodies (like sodium cyanide lobeline and coramine) alone it is barely capable of doubling ventilation An increased oxygen tension in the plasma (p O) does not inhibit respiration Oxygen tension of course is an expression of the amount of oxygen dissolved in the plasma and in arterial blood is nearly equal to the partial pressure of oxygen to which the plasma has been exposed in its journey through the lungs i e to the partial pressure of oxygen in alveolar air The partial pressure of oxygen in the atmosphere is about 21 per cent of the barometric pressure = 21 per cent of 760 mm Hg = 159 mm Hg In alveolar air the gas mixture is not the same as in the atmosphere for it is almost fully saturated with water vapour contains about 5 6 per cent of carbon dioxide which it has collected from the plasma and is left with only 14 2 per cent of oxygen The partial pressure of oxygen in alveolar air should therefore be 14 2 per cent of 760 mm Hg or allowing for water vapour 14 2 per cent of (760—47) = 101 2 mm Hg That the arterial oxygen tension (90 to 95 mm Hg) is not the same is due to slight perfusion of unventilated alveoli The oxygen tension of venous blood is only about 40 mm Hg so that there is a strong oxygen pressure gradient across the interface between the alveolar wall and the proximal end of the pulmonary capillary favouring rapid diffusion The plasma oxygen tension determines whether hæmoglobin takes up oxygen or releases it The familiar oxygen dissociation curve of hæmoglobin shows the changing affinity that hæmoglobin has for oxygen according to the oxygen tension of the plasma at high tensions around 100 mm Hg hæmoglobin is 95 per cent saturated with oxygen, as the tension falls towards 70 mm Hg the proportion of oxyhæmoglobin declines very little

to about 90 per cent as the oxygen tension falls below 70 mm Hg however hæmoglobin appears more and more in its reduced form so that at an oxygen tension of 40 mm Hg, which is average for venous blood hæmoglobin is only about 70 per cent saturated and at a tension of 30 only about 50 per cent saturated this behaviour makes hæmoglobin an ideal vehicle for transporting oxygen storing it when plentiful and releasing it where it is most wanted

CARBON DIOXIDE stimulates the respiratory centre directly and is capable of increasing ventilation tenfold Again it is the tension of carbon dioxide in the arterial blood (p CO_2) that matters and this is equal to the partial pressure of carbon dioxide in alveolar air for this gas diffuses far more rapidly in fluid media than oxygen The partial pressure of alveolar CO is normally about 5 6 per cent of (760−47) mm Hg = 40 mm Hg approximately Thus the arterial CO_2 tension is also 40 mm Hg A rise of only 2 5 mm Hg in arterial CO tension is enough to double ventilation (Gray 1950) a fall in p CO depresses the respiratory centre

Like oxygen carbon dioxide is formed in too great a quantity to be transported as a simple solution in plasma and so it too has a special means of conveyance Hæmoglobin is again made use of Carbon dioxide from the tissues diffuses into the venous blood at a tension around 46 mm Hg and readily enters the red corpuscles Here with the aid of an enzyme carbonic anhydrase it joins with water to form carbonic acid H_2CO_3 This combines with potassium base obtained from reduced hæmoglobin thus



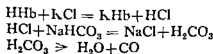
$$H\,CO_3 + KHb = HHb + KHCO_3$$

because carbonic acid is a stronger acid than reduced hæmoglobin Dissociation allows bicarbonate anions (HCO_3) so formed in the cells to diffuse out into the plasma leaving unattached potassium kations (which cannot pass the cell membrane) within the corpuscles Equilibrium is restored by the well known chloride shift dissociation of sodium chloride in the plasma allowing sodium+ to combine with HCO_3 to form plasma bicarbonate, while chloride anions pass into the red cells to combine with potassium



$$K^+ \; HCO_3^- \qquad Na^+ \; Cl^-$$
$$KCl \qquad NaHCO_3$$

When the red cells reach the lungs the chloride shift is reversed because oxyhæmoglobin is a much stronger acid and promptly re acquires the potassium base thus releasing chloride from the cells the chloride combines with the sodium of the plasma bicarbonate to form the weaker acid $H\,CO_3$ from which carbon dioxide is finally excreted through the lungs thus



$$HHb + KCl = KHb + HCl$$
$$HCl + NaHCO_3 = NaCl + H_2CO_3$$
$$H_2CO_3 \geqslant H_2O + CO$$

It follows that *an increase of carbon dioxide in the blood results in an increase of*

plasma bicarbonate When the carbon dioxide of the body is depleted as by forced breathing the plasma bicarbonate falls In other words *carbon dioxide is carried as bicarbonate* in the plasma

Since the plasma bicarbonate is the most important buffer substance available for neutralising fixed acid such as lactic acid it has been called the *alkali reserve* This may be measured by finding out how much carbon dioxide is liberated from the plasma under controlled conditions when exposed to an acid the answer being expressed in volumes (ml) per cent The normal *carbon dioxide content* of plasma is 53 to 75 volumes per cent when measured in this way This is often called the *carbon dioxide combining power* or *carbon dioxide capacity* of the plasma The terms *acidosis* and *alkalosis* refer to states in which the carbon dioxide content of the plasma is below 53 or above 75 volumes per cent respectively This has caused much confusion for every clinician knows that forced breathing which results in CO_2 washout causes a transient slight rise in pH (alkalæmia) yet the reduction in alkali reserve (carbon dioxide content) to which it also gives rise, entitles it to be called a state of acidosis Again in advanced cor pulmonale particularly if ventilation is depressed by any means a high CO_2 tension may be associated with a lowered pH (acidæmia) and increased alkali reserve (alkalosis) The confusion would be avoided if the terms acidæmia and alkalæmia were used (as now) to denote a fall or rise of pH and the terms acidosis and alkalosis were dropped altogether in favour of more precise designations for the plasma bicarbonate

A less variable and more informative figure is the carbon dioxide content of arterial blood which in health is 45 to 53 ml per cent

A final very important point about the carbon dioxide tension as a respiratory stimulant is the narcotic effect produced when the tension exceeds 60 mm Hg At such levels carbon dioxide may not only cause unconsciousness but actually depresses the respiratory centre As will be seen later the treatment of cor pulmonale with oxygen is much influenced by this consideration

THE HYDROGEN ION CONCENTRATION or pH value is the third important respiratory stimulant and like carbon dioxide acts directly on chemo receptors in the respiratory centre The normal pH is given as 7 41 it remains remarkably constant in health and is one of the last things to alter in disease It is maintained largely by the buffer systems of the blood by removal of an ever varying quantity of carbon dioxide by the lungs and by excretion of acid or alkaline substances in the urine The chief effect of the buffer systems such as the plasma bicarbonate is to ensure as far as possible that no acid stronger than H_2CO_3 can exist in the blood For example lactic acid derived from working muscle is at once converted by sodium bicarbonate into sodium lactate and carbonic acid Any increase of CO_2 tension resulting from the exchange at once stimulates the respiratory centre and excess CO_2 is removed via the lungs Nevertheless metabolic disturbances do occur in diabetes mellitus for example in which a reduced

pH causes hyperventilation in such cases the carbon dioxide tension will also be reduced (as a result of increased CO_2 washout) An increased CO_2 tension itself also causes slight reduction of the pH

MUSCULAR EXERCISE is a respiratory stimulant independent of secondary changes in CO_2 tension

HEAT is also an important respiratory stimulant Thermoreceptors in the hypothalamus react to changes in body temperature and explain the hyperventilation of high fever Thermoreceptors in the skin react to change in the temperature of the environment

The *inter relationships* between these various respiratory stimuli are complicated and cannot be discussed here but when considering the effect of any one of them it is most important to consider at the same time what is happening to the others For example with very high CO tensions in advanced cor pulmonale, the respiratory centre may be responding only to oxygen lack as previously explained If the patient is nursed in an oxygen tent the only stimulant to respiration may be abolished and ventilation may greatly decline This reduces excretion of carbon dioxide and the patient may become unconscious from CO narcosis

So much then for the central control of respiration We now have to consider the physiology of ventilation itself, i e the events that take place in the lungs to ensure proper oxygenation of perfusing blood and elimination of carbon dioxide

VENTILATION

In what is called a *steady state* the amount of oxygen taken up by the lungs exactly equals the amount utilised by the tissues minute by minute and the amount of carbon dioxide eliminated by the lungs exactly equals that formed in the tissues The amount of oxygen consumed varies with the surface area of the body, which can be obtained from tables of height and weight and is called the metabolic rate It is usually around 250 ml per minute, and if measured under basal conditions is called the *basal metabolic rate* being expressed as a percentage of normal To every 250 ml of oxygen consumed, about 200 ml of carbon dioxide is eliminated The ratio in this example $\frac{200}{250} = 0\ 80$ is called the *respiratory quotient*

Resting ventilation

For each 100 ml of oxygen consumed about 2 5 litres of air must be breathed This ratio is the *ventilation equivalent for oxygen* If 250 ml of oxygen have to be absorbed per minute, then at this equivalent 6 25 litres *of air must be breathed* This is the resting ventilation and is the *tidal volume* (about 500 ml) multiplied by the number of inspirations per minute (in this case 12 5) and can be measured very simply with
It is the respiratory analogy of the cardiac output at -

Reserves

From a state of quiet breathing it is always possible to inspire much more deeply this extra depth of a single maximum inspiration is the *inspiratory reserve* (2 to 2 5 litres) The term *inspiratory capacity* (or complemental air) refers to the sum of the tidal volume and the inspiratory reserve it is the maximum inspiration after quiet expiration The *expiratory reserve* (or supplemental air) is the maximum volume of air that can be expelled after quiet expiration (usually 1 to 1½ litres)

Vital capacity

The sum of the tidal inspiratory reserve and expiratory reserve volumes is the vital capacity It should measure around 3 5 to 4 5 litres

Total lung volume (or capacity)

After maximum expiration there is still a good deal of air in the bronchial tubes and trachea this is known as the dead space or *residual volume* and in disease may include parts of the lung that cannot be deflated It is possible to measure the dead space plus the expiratory reserve volume during quiet breathing the sum of the two being called the *functional residual capacity* (air or volume) by finding out how much a known quantity of an inert gas such as helium is diluted when introduced into a closed circuit comprising the air in the spirometer and the space to be measured The residual volume of course is the functional residual capacity so determined less the expiratory reserve volume as measured directly with a spirometer The *total lung volume* is the residual volume plus the vital capacity or the functional residual capacity plus the inspiratory capacity In health the residual volume measures 1 to 1½ litres and the total lung volume about 5 litres The various divisions of the lung volume are shown diagramatically in figure 5 16 A useful ratio is the residual volume expressed as a percentage of the total lung capacity (normal 20 to 25 per cent) According to Motley (1950) this measurement correlates well with the degree of emphysema present

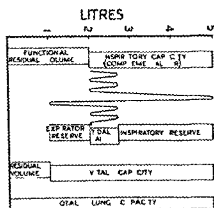


Fig 5 16—Subdivisions of the lung volume

Maximum breathing capacity

One of the most important measurements of lung function is the maximum breathing capacity which is the maximum volume of air that can be ventilated per minute It can be measured with a spirometer provided sufficient attention is paid to eliminating resistance Maximum

forced breathing is continued for 15 seconds and the result expressed in litres per minute There is a wide normal range scattering around 75 to 100 litres per minute

The *breathing reserve* is the maximum breathing capacity less the resting ventilation per minute As pointed out by Donald (1953) much of this so called reserve can never be used for even normal subjects are uncomfortably dyspnœic when using 50 to 60 per cent of their maximum breathing capacity It may be better simply to express the actual ventilation per minute as a percentage of the maximum breathing capacity

Mixing efficiency

In normal lungs all functioning alveoli are ideally supplied with an equal quantity of inspired air and each is perfused with blood from the pulmonary arteries non functioning alveoli are collapsed and are not perfused related capillaries temporarily shutting down In disease, however this is not necessarily so unperfused alveoli may be supplied with air and perfused alveoli may not be so supplied When all parts of the lung are properly ventilated an inert gas like helium when introduced to a closed spirometer lung circuit quickly attains uniform distribution after which no further dilution occurs If parts of the lung contain stale air which is not moved to and fro however efficient mixing is delayed, and dilution of helium takes longer to reach a static level The speed at which an inert gas attains maximum dilution is therefore a measure of mixing efficiency but allowance must be made for a number of variables which influence the rate of mixing such as the minute volume of respiration at the time (Bates and Christie 1950)

Unventilated perfused alveoli necessarily lead to a fall in oxygen tension and content of arterial blood But a similar degree of oxygen unsaturation of arterial blood may result from difficulty in oxygen diffusion across the interface between alveolus and capillary as in diffuse fibrosis of the lung In this group of cases however mixing efficiency is normal

Poorly ventilated space

When the concentration of helium is plotted against time in normal subjects a smooth dilution curve is constructed which at first falls away rapidly and then gradually straightens out until horizontal When mixing is inefficient owing to parts of the lung being underventilated rapid dilution is checked early the initial steep slope suddenly assuming a more gentle gradient This point signals complete mixing in all properly ventilated parts of the lung the rest of the curve representing slower mixing in poorly ventilated spaces From the concentration of helium at the moment its dilution is checked the volume of properly ventilated lung can be calculated this subtracted from the total lung volume gives the volume poorly ventilated space

Diffusion gradients

Owing to the extremely high rate of carbon dioxide diffusion in fluids, the arterial p CO_2 is always virtually the same as that in the alveoli (Riley and Cournand, 1951). The oxygen tension in the alveoli and the p O_2 of blood leaving the pulmonary capillaries however is not necessarily the same although it has been shown to be so in health (Lilienthal *et al* 1946), minor differences between alveolar and arterial p O_2 being due to slight *venous admixture* i e to a little perfusion of unventilated alveoli.

The alveolar oxygen tension may be calculated from the formula

$$\text{Alveolar p } O_2 = \text{p } O_2 \text{ in inspired air} - \frac{\text{alveolar p } CO_2}{\text{resp quotient}}$$

as quoted by Donald (1953). This formula is based on two important observations (1) the differences in partial pressure between O_2 and CO_2 in the inspired air and alveolar air are proportional to the quantities of these gases consumed and excreted so that

$$\text{R Q or } \frac{CO_2 \text{ eliminated}}{O_2 \text{ absorbed}} = \frac{\text{alv p } CO_2 - \text{insp p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

and since the partial pressure of CO_2 in inspired air is negligible

$$\text{R Q} = \frac{\text{alv p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

and (2) the alveolar CO_2 tension is the same as that in arterial blood as previously stated so that

$$\text{R Q} = \frac{\text{arterial p } CO_2}{\text{insp p } O_2 - \text{alv p } O_2}$$

$$\text{Alv p } O_2 = \text{insp p } O_2 - \frac{\text{art p } CO_2}{\text{R Q}}$$

Now the partial pressure of oxygen in the inspired air which is fully saturated with water vapour is about 21 per cent of $(760-47) =$ 150 mm Hg. Thus in normal subjects

$$\text{the alveolar oxygen tension} = \text{(say) } 150 - \frac{40}{0.8} \text{ mm Hg}$$
$$= 100 \text{ mm Hg}$$

Assuming the arterial oxygen tension is 95 mm Hg this gives an alveolar arterial oxygen tension gradient of 5 mm Hg which represents the admixture of a small quantity of unventilated perfused venous blood.

The technique of these measurements of lung function must be sought in standard works on lung physiology. The basic principles involved and the terminology employed have been described here in some detail in order to help clinicians understand what the respiratory physiologist is about and what the various respiratory tests to which his patients may be subjected really mean.

APPLICATIONS

Briefly *emphysema* is as a rule characterised by a normal or even increased total lung volume increased residual volume diminished vital capacity diminished inspiratory reserve greatly diminished maximum breathing capacity increased resting ventilation poor mixing efficiency large poorly ventilated space and in advanced cases by reduction of arterial oxygen tension and saturation and an increase of arterial carbon dioxide tension and content

Pulmonary fibrosis in various forms is characterised especially by a raised alveolar arterial oxygen tension gradient and in advanced cases by a reduced arterial oxygen saturation ventilation being more or less normal and the arterial CO_2 content normal or low

Pulmonary venous congestion ' from left heart failure or mitral stenosis behaves rather like pulmonary fibrosis in respect of its effect on lung function

Bronchospasm pneumonia atelectasis large pleural effusion spontaneous pneumothorax and other space filling lesions interfere chiefly with ventilation

RENAL FUNCTION TESTS

Testing the urine for albumin and sugar microscopic examination of the urinary sediment (particularly for red cells and casts) bacteriology when indicated urine concentration tests blood urea urea concentration and clearance and intravenous pyelography usually give sufficient information to satisfy the cardiologist but the glomerular filtration rate as measured by inulin or creatinine clearance and the plasma blood flow as measured by diodone or para amino hippuric acid clearances are useful refinements Renal function is particularly important in all hypertensive states congestive heart failure bacterial endocarditis and certain collagen diseases

The *water concentration test* consists simply of withholding all fluids for a maximum of 36 hours (starting at 6 p m) or until the specific gravity of the urine is 1027 at room temperature This is a very simple yet sensitive test of the power of the tubules to reabsorb water The more damaged the kidney in hypertension the more nearly does the urine resemble the glomerular filtrate and in the end its specific gravity is the same as that of the plasma being fixed at 1010

Urea concentration is another test of tubular function After ingesting 15 G of urea a normal individual should pass urine having a urea concentration of at least 2 G per cent The dose is taken immediately after emptying the bladder and urine is then voided after one and again after two hours the second specimen being the more important since diuresis may interfere with concentration during the first hour

A *blood urea* higher than 45 mg per cent indicates considerable impairment of glomerular filtration In uremia of course it may rise as high as 500 mg per cent The *blood creatinine* normally 0 7 to 2 mg per

rises sharply in uræmia, and may reach 5 or even 10 mg per cent Creatinine is normally concentrated to about 75 mg per cent in the urine

A *clearance test* measures the amount of blood or plasma passing through the glomeruli or tubules which is cleared of a particular substance per minute In the familiar urea clearance test of Van Slyke the concentration of urea in the blood and urine, and the volume of urine formed each minute are measured suppose the urine flows at a rate of 2 ml per minute and each ml contains 20 mg of urea (concentration 2 G per cent) then the quotient 40 mg per minute represents the quantity of urea filtered from the blood If the blood urea at the time was 0.4 mg per ml (40 mg per cent) then the amount of blood filtered of urea must have been $\frac{40}{0.4} = 100$ ml Thus we have the simple formula clearance $= \frac{UV}{B}$

where U is the concentration of the substance in the urine
V is the volume of urine formed per minute
and B is the concentration of the substance in the blood

In the case of urea there are two important considerations (1) blood passing through the glomeruli is not completely cleared of urea so that the test does not measure the actual amount of blood passing through the glomeruli but the amount that would have passed had it been totally cleared (2) urea is partly reabsorbed by the tubules particularly when its concentration there is high, as it is likely to be when the urine flow is reduced and under these circumstances Van Slyke found more consistent results were obtained when the formula was changed to

$$\text{urea clearance} = \frac{U\sqrt{V}}{B}$$

The result is expressed as a percentage of normal Average *normal* urea clearances were found to be 75 ml per minute when the urine flow was 2 ml or more per minute and 54 (using the square root of V in the formula) when the urine flow was less than 2 ml per minute Thus when the *standard* urea clearance is reported as 50 per cent of normal it means that the actual clearance was one half of 54 or 26 ml per minute if the word *maximum* is added it means that the flow was 2 ml per minute or more and that the actual clearance was one half of 75 or 37.5 ml per minute

Inulin has the advantage of being filtered freely by the glomeruli but not reabsorbed by the tubules at all (Smith 1939–40) The plasma inulin clearance is measured in exactly the same way, the formula being $C = \frac{UV}{P}$ plasma concentration is substituted for blood concentration because inulin does not penetrate the red cell The average normal plasma inulin clearance is 120 ml per minute This test has another meaning however for since inulin is filtered freely its concentration in the glomerular filtrate is precisely

the same as its concentration in the plasma and since it is not reabsorbed by the tubules the clearance figure determines the amount of filtrate actually formed and may be justly called the *glomerular filtration rate*

Endogenous creatinine clearance is also a good test of filtration but not so reliable as inulin (Brod and Sirota 1948) Typical figures are

$$\text{Creatinine clearance} = \frac{UV}{B} = \frac{80 \text{ mg per cent} \times 1.5 \text{ ml per minute}}{1 \text{ mg per cent}}$$

$$= 120 \text{ ml per minute}$$

The *total renal blood flow* may be estimated in two ways If the urea content of blood samples from the renal artery and vein are known and the amount of urea excreted in the urine per minute is known then since the amount lost from the blood must equal the amount in the urine

$$\text{renal blood flow} = \frac{UV}{\text{arterio venous urea difference}}$$

$$= (\text{say}) \frac{2\,000 \text{ mg per cent} \times 2 \text{ ml per minute}}{30-26 \text{ mg per cent}}$$

$$= 1\,000 \text{ ml per minute}$$

Renal vein samples may be obtained by means of venous catheterisation and any substance excreted by the kidney may be used instead of urea In fact urea is not very suitable because of its variable rate of excretion creatinine serves very well

The second method is based on the fact that certain substances like diodone and para amino hippuric acid are totally excreted by the tubules when their blood concentration is sufficiently low so that their clearance rates then genuinely represent the *renal plasma flow* itself (Smith 1939–40)

Milli equivalents

The quantity of any substance in whole blood plasma or serum is usually reported in mg per cent or milli equivalents The latter term is used in respect of electrolytes such as sodium potassium and chloride which occur in an ionic form in the plasma The equivalent weight of a sub stance is that weight of it which will combine with or displace one gramme atom of hydrogen and a milli equivalent is this weight divided by a thousand The equivalent weights of monovalent ions like sodium are the same as their atomic weights e g 23 for sodium so that one *milli equivalent* of sodium weighs 23 mg Thus if the serum sodium is 320 mg per cent it may be expressed as $\frac{320 \times 10}{23} = 139$ milli equivalent per litres

The advantage of this system is that the unit of any substance is chemically equivalent to the unit of any other substance a statement that would not be true if applied to a unit of metric weight like a milligram

Electrolytes

An electrolyte is any substance which in greater or less degree dissociates into its constituent ions when dissolved in water Thus sodium chloride dissociates into sodium cations (positive) and chloride anions (negative) or Na^+ Cl^- potassium chloride into K^+ Cl^- sodium bicarbonate into Na^+ HCO_3^- and so on The most important substances of this kind are sodium, potassium, chloride and bicarbonate and their normal concentrations in the serum are given below

	Mg per cent (unless otherwise stated)	*M eq per litre*
Serum sodium	310 to 345	135 to 150
Serum potassium	15 to 21	4 to 5
Plasma chlorides	340 to 390	95 to 110
Plasma bicarbonate	53 to 77 vols of CO per cent	25 to 35

PHONOCARDIOGRAPHY

Special techniques fall into two major groups those that give information of a kind that cannot be obtained otherwise such as radiology electrocardiography and cardiac catheterisation and those that offer a more accurate or standardised means of measuring or recording phenomena which can be recognised qualitatively in other and usually simpler ways such as sphygmomanometry polygraphy and kymography Although phonocardiography belongs to the second group it has contributed much to our knowledge and understanding of heart sounds and murmurs and has provided us with a practical tool with which to solve difficult auscultatory problems

The heart sounds were first visually recorded by Frank (1904) using a stethoscopic chest piece pneumatic connection mirror capsule (q v) and optical recording a relatively simple method perfected by Orias and Braun Menendez (1939) Einthoven (1907) substituted a carbon microphone (q v) for the capsule and let it actuate a string galvanometer More recently the stethoscopic chest piece has been replaced by a Rochelle salt crystal microphone (q v) which converts sound pressure waves into proportionate electrical charges these are amplified and led to a suitable string or mirror galvanometer (Leatham 1949)

Picked up in this way the intensity of heart sounds and murmurs bears little relation to what is actually heard through a stethoscope low frequency sounds having a very much higher amplitude than high frequency sounds This means that with linear recordings and amplification adjusted so that a high pitched murmur would show suitably in the tracing a low pitched third heart sound would throw the galvanometer beam off the record The human ear is nicely adjusted to this phenomenon and while being

remarkably sensitive to sound frequencies around 2 000 to 3 000 cycles per second it is logarithmically less sensitive to sounds of decreasing frequency until at 15 cycles per second it does not respond at all at the other end of the scale the highest frequency that can be heard is 20 000 to 30 000 cycles per second varying with the individual In phonocardiography it is usually desirable to record not only what is actually heard but also what is on the threshold of hearing Records having a linear response to sound intensity at all frequencies are impracticable, as already explained The intensity of low pitched sounds must be attenuated to bring them more into line with the weaker high pitched sounds so that both may be recorded in the same tracing This is achieved by incorporating filters (condensers and resistances) in the amplifying circuit Three degrees of low frequency attenuations have been found most useful in the first or low frequency response damping of low frequency sounds is minimal and

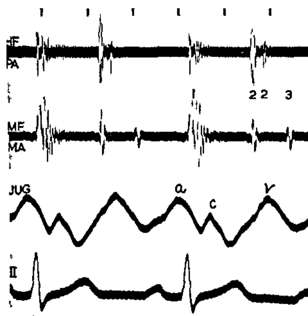


Fig 5 17 —Normal phonocardiogram taken from apex and base recorded simultaneously with the electrocardiogram and the jugular phlebogram Time marking 0 04 and 0 2 sec Split first and second heart sounds best seen in high frequency tracing from the pulmonary area (top graph)

With acknowledgments to Dr Aubrey Leatham

amplification has to be reduced so that low pitched sounds such as the third heart sound and soft mitral diastolic murmurs are well seen at the expense of high pitched sounds which may be insufficiently amplified to appear at all in the second or medium frequency record moderate attenuation of low pitched sounds allows greater amplification of high pitched

sounds and murmurs so that these also can be seen in the third or high frequency response, sounds of low frequency are greatly weakened allowing greater amplification and recording of high pitched murmurs This last kind of record is similar to the logarithmic curve of Rappaport and Sprague (1941 1942) and may be called ear like for it closely resembles what is actually heard (Leatham 1949)

The galvanometer must be sensitive to frequencies of at least 1 000 cycles per second preferably to 2 000 if the highest pitched aortic diastolic murmurs are to be recorded faithfully Most systolic murmurs have a frequency around 200 to 400 cycles per second mitral diastolic murmurs 50 to 200 cycles per second and the lower pitched heart sounds 16 to 50 cycles per second (Leatham 1949) Theoretically the cathode ray oscillograph would seem the most suitable instrument for recording heart sounds in view of its almost unlimited frequency response but in practice it has been found less satisfactory partly on account of base line wobble and rather hazy photographs

Phonocardiograms should be recorded simultaneously with an electrocardiogram jugular phlebogram or some other reference tracing so that sounds and murmurs may be accurately timed against recognisable events in the cardiac cycle one of the best reference tracings is actually a second phonocardiogram from a different site (fig 5 17)

The various heart sounds and murmurs that may be recorded in health and disease together with their timing and pitch have already been described in detail in Chapter II and time relationships with other events in the cardiac cycle are illustrated in figure 5 15

BALLISTOCARDIOGRAPHY

When a gun is fired it recoils This illustrates Newton s third law of motion which states that for every action on a body there is an equal and opposite reaction When a patient with gross aortic incompetence is lying in bed every clinician knows that the bed may rock—footwards during initial systolic ejection and headward as blood courses down the descending aorta As early as 1877 Gordon recorded the movements of a suspended platform on which a man was lying—the first ballistocardiogram Henderson (1905) suggested that there should be a relationship between such recoil movements of the body and the stroke output of the heart The principle was introduced into clinical medicine in 1939 by Starr and his associates Since one of the basic principles of all forms of manometry is that the natural oscillating frequency of a manometer should be well outside the frequency range of the phenomenon being recorded Starr *developed a couch with a natural frequency of 12 to 14* cycles per second when suitably loaded (Starr 1941 1946) which is two and a half times the natural frequency of the human body (3 to 7 cycles per sec) The bed moves with body recoil such movements being suitably amplified and recorded Nickerson and Curtis (1944) designed a low frequency bed with

a natural oscillation of 1 5 cycles per second critical damping is employed to keep the natural frequency at 1 5 whatever the weight of the patient In the ballistocardiograph designed by Dock and Taubman (1949) the body is allowed to move on its own cushion of fat, the movements of a bar laid across the shins being amplified and recorded A great deal of work particularly in the U S A, has been done on the ballistocardiograph in recent years, and has been well reviewed by Scarborough *et al* (1952) and Gubner (1953) An important aspect of this basic research has been the realisation that the forces of acceleration and deceleration are primarily responsible for the ballistic effect

Clinical ballistocardiogram

The chief waves of the ballistocardiograms are H I J and K (fig 5 18) H is a relatively small initial headward deflection probably due to venous deceleration at the end of diastole I is the first strong downward deflection and is due to recoil from acceleration of blood in the ascending aorta and pulmonary arteries being synchronous with the rapid ejection phase J is the maximum deflection and is upright it is associated with acceleration of blood in the descending aorta the body recoiling headwards it is synchronous with the main pulse wave of the body K is a fairly strong downward movement and has been attributed to deceleration of blood in the descending aorta due to the impact of the pulse wave at the periphery it disappears in coarctation of the aorta and is augmented in aortic incompetence It must be admitted however that there is no universal agreement about the true origins of these waves

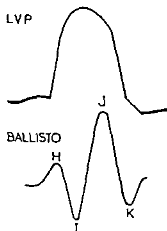


Fig 5 18—Diagram of a normal ballistocardiogram to show approximate time relationship to the left ventricular pressure pulse (see text)

Various formulæ for estimating the stroke output by measuring the height or area occupied by I and J have been devised by Starr and others and modified to give results comparable to those found by methods employing the Fick principle (Scarborough *et al* 1952)

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CHAPTER VI

DISORDERS OF CARDIAC RHYTHM

THE speed and regularity of the heart beat are controlled by the sino atrial node of Keith and Flack (1907) situated in the upper part of the sulcus terminalis anterior to and to the right of the mouth of the superior vena cava (fig 6 01) Approximately 70 times per minute this node discharges itself and initiates an excitation wave which spreads in all directions over both atria Close to the opening of the coronary sinus above the base of the tricuspid valve on the right side of the atrial

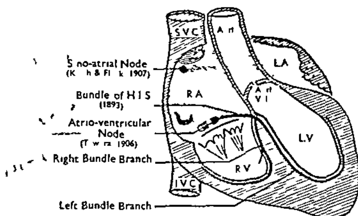


Fig 6 01—Anatomy of the conducting system

septum is situated the atrio ventricular node of Tawara (1906) This also forms impulses but at a slower rate so that normally it is prematurely discharged by the excitation wave initiated by the S A node The impulse then spreads down the Bundle of His which passes horizontally to the left to penetrate the membranous interventricular septum where it divides into left and right bundle branches These pass down each side of the muscular septum just beneath the endocardium The bundle branches then break up into a network of Purkinje fibres which carry the excitatory process to the sub endocardial myocardium

Physiology of conduction From the pace maker in the sino atrial node the excitation wave spreads through atrial muscle at a speed of about 1 000 mm per second Passage through the A V nodal tissue is believed to be relatively slow and is estimated at 200 mm per second Spread down the bundle branches and the Purkinje fibres is rapid and is probably as

fast as 400 mm per second Conduction through the ventricles which is believed to proceed directly outwards is put at 400 mm per second (Lewis 1925)

Both the S A and A V nodes are under direct autonomic control being stimulated by sympathetic activity and depressed by vagal activity Cardiac accelerator nerves arise from the lateral horns of the upper 4th or 5th dorsal segments of the spinal cord enter the sympathetic chain and pass cranially to the cervical ganglia Post ganglionic fibres form the superior middle and inferior cardiac nerves which terminate in the S A and A V nodes

IRREGULARITIES AND ALTERATION OF HEART RATE INITIATED OR GOVERNED BY THE SINO ATRIAL NODE

SINUS ARRHYTHMIA

There is probably no such thing as an absolutely regular heart Slight irregularity the heart quickening with inspiration and slowing with expiration is normal and depends upon variations in vagal tone governed by a reflex which is thought to be initiated by receptors in the lungs Another form of sinus arrhythmia occurs independently of respiration Both are more common in the young and when the heart rate is slow tend to be exaggerated by drugs that increase vagal tone (such as digitalis) and may be abolished by exercise or atropine

Other varieties of sinus arrhythmia are not essentially different but owe their recognition to some particular associated feature thus there is a form

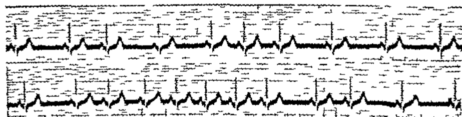


Fig 6 02—Sinus arrhythmia

associated with sino atrial block another with sinus bradycardia and paroxysmal auricular fibrillation or flutter a third with convalescence from certain infectious fevers especially influenza and so on Increased vagal tone is common to all these types

Diagnosis is usually easy or doubt is soon resolved by means of exercise atropine, or amyl nitrite An electrocardiogram provides conclusive evidence (fig 6 02)

Although sinus arrhythmia is normal it should not be regarded as a positive sign of a normal cardiovascular system for it may occur in any form of heart disease

SINUS TACHYCARDIA

The heart rate varies markedly in different mammals In the elephant for example it is about 30 beats per minute in the rat it is close on 600 It is considerably slower in the hare than in the rabbit On the whole the speed is inversely proportional both to the size and to the athletic endurance of the animal In man the average heart rate is 72 beats per minute but there are wide limits of normality ranging between 40 and 100 The pulse is faster in children averaging 120 to 130 at birth and slowing gradually during childhood to reach about 80 at puberty The more athletic the individual the slower the pulse as a rule and in well trained athletes resting figures of 45 to 50 are common It follows that tachycardia may mean a heart rate faster than average faster than the upper limit of normality or faster than what is known to be normal for a particular individual

Applied physiology Tachycardia has always played an impressive part as a physical sign in general medicine It has received weighty consideration in fevers in all forms of heart disease in shock and hæmorrhage in various chronic diseases such as pulmonary tuberculosis and indeed in almost every condition yet it can mean little unless its immediate cause is under stood This is not to decry tachycardia as a valuable sign but to emphasise that its significance depends upon its mechanism

The speed of the sino atrial pace maker is strongly influenced by the autonomic nervous system Complete paralysis of the vagus may be produced within a minute by giving 2 to 3 mg of atropine sulphate intra venously whereupon the heart accelerates to a speed of 130 to 160 per minute The cardiac output per minute rises simultaneously but the fall in venous filling pressure that accompanies the tachycardia may counteract this effect (McMichael and Sharpey Schafer 1944) The ventricular stroke volume is diminished even in those with higher outputs Emotional tachy cardia as in the anxiety states and the tachycardia of convalescence appear to be due to diminished vagal tone

Tachycardia may be due to a rise in pressure within the great veins and right atrium venous receptors initiating the Bainbridge reflex by which vagal tone is reduced Under these circumstances the stroke-volume may be maintained or increa ed the cardiac output per minute rising in pro portion to the tachycardia or even higher This mechanism operates during effort and in anæmia beri beri arteriovenous shunt anoxic pulmonary heart disease generalised active Paget s disease and pregnancy The Bai bridge reflex is also partly responsible for the tachycardia so freq seen in congestive failure

The speed of the heart is also controlled by reflexes initiated by baro receptors in the aorta and carotid sinuses When the blood pressure rises vagal tone is increased and the heart slows when it falls vagal tone is diminished and the heart quickens (Marey s Law). This is the mechanism of the bradycardia associated with conditions causing a transient rise of blood pressure such as acute nephritis and it is part of the mechanism controlling the tachycardia of low blood pressure states

Anoxia may cause tachycardia by direct action on the central nuclei or possibly reflexly through the carotid sinus Just what part it plays in the production of tachycardia in anæmia and cor pulmonale is uncertain Thyroxin and fever have a direct stimulating action on the pace maker and so has adrenaline, but the latter may also excite the carotid sinus slowing reflex by raising the blood pressure so that the heart rate may change but little The elevated cardiac output that accompanies the tachycardia is also probably due in part to a direct action on the heart In the case of adrenaline the cardiac output may rise when there is no change in heart rate or blood pressure (McMichael and Sharpey Schafer 1944)

Differential diagnosis From the clinical point of view sinus tachycardia must be distinguished from auricular flutter and from paroxysmal tachy cardia This is usually possible at the bedside Sinus tachycardia varies in rate from minute to minute, or at least from hour to hour and it varies with emotion effort and change of posture Carotid sinus or eyeball com pression and release result in gradual rather than abrupt slowing and quickening of the pulse respectively although changes may be difficult to detect with fast rates In auricular flutter (and sometimes in paroxysmal auricular tachycardia) the rate is usually fixed neither varying spon

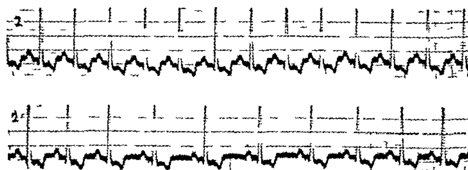


Fig 6 03—Sinus tachycardia slowed by carotid sinus compression

taneously nor with emotion, effort, or change of posture whilst on carotid sinus pressure slowing is abrupt often to half the rate 2 1 physiological atrio ventricular block being converted into a 4 1 relationship and on release reversion to the original rhythm is again abrupt and may not take place for several seconds Even without so precise a clinical analysis, the

degree of slowing may yet be too gross for sinus tachycardia In paroxysmal nodal and ventricular tachycardia the rate is also fixed, and carotid sinus pressure either stops the attack abruptly as in 50 per cent of the nodal cases or has no effect whatever If it is impossible to interpret the results of carotid sinus pressure clinically the problem may be solved by combining the manœuvre with an electrocardiogram (fig 6 03) It should be explained that an electrocardiogram *per se* may not afford certain distinction between these three rhythms although lead V_1 or CR_7 greatly facilitates analysis

Effect on the heart Sinus tachycardia presents an important problem in relation to heart failure Is it a causal factor or merely a reflection of cardiac embarrassment? Or is it part of a compensatory adjustment beneficial under the circumstances? Such questions are difficult to answer directly but the presentation of some of the relevant facts may help to clarify the issue A normal heart tolerates any natural degree and duration of sinus tachycardia rates approaching 200 for example being common during violent exertion and persistent rates of 120 or so being endured for over 20 years in certain cases of Da Costa s syndrome without harmful results On the other hand diseased hearts frequently develop congestive failure with heart rates of 150 to 200 in auricular flutter or paroxysmal tachycardia the effect being attributed to overwork and fatigue resulting from insufficient diastolic rest The tachycardia of the hyperkinetic forms of cardiovascular disorder (thyrotoxicosis anæmia anoxic cor pulmonale beri beri arterio venous aneurysm and generalised Paget's disease) is part of the physiological mechanism maintaining a high cardiac output and therefore performs a useful function but when the heart fails i e when it is overloaded the cardiac output falls and the tachycardia is wasted Under such circumstances tachycardia reflects cardiac embarrassment and deprives the heart of diastolic rest In the hypokinetic forms of heart failure such as those which may be seen in cases of hypertension and mitral stenosis tachycardia due to the Bainbridge or carotid sinus reflex is a reflection of cardiac distress from the start and serves no useful purpose In chronic constrictive pericarditis and to a lesser extent in high pressure pericardial effusion tachycardia may provide the only means of maintaining an adequate cardiac output for the stroke volume is strictly limited In the active forms of carditis (rheumatic diphtheritic and Fiedler s) and in bacterial endocarditis the heart rate may be disturbed by local pathology fever, toxæmia or (in diphtheria) by circulatory collapse and probably adversely affects the heart On the whole it may be said that the heart tolerates sinus tachycardia which tends to deprive it of rest better than a high cardiac output and much better than a raised blood pressure both of which increase its work

There is no treatment for sinus tachycardia itself but attention should be paid to its cause

SINUS BRADYCARDIA

As already stated, heart rates of 45 to 50 per minute are common in athletes Some individuals irrespective of their physical training have a naturally slow pulse Sinus bradycardia is a feature of certain diseases, notably myxœdema and obstructive jaundice and is not uncommon during convalescence from certain fevers especially influenza It also occurs when the blood pressure is raised rather suddenly as in acute nephritis the slowing being reflex through the sino aortic afferents and vagus It is a familiar sign of lesions that increase the intracranial pressure when it may be due to direct stimulation of central nuclei Slowing of the pulse may be induced temporarily by carotid sinus or eyeball pressure as a transient event it occurs naturally in vaso vagal syncope

The differential diagnosis between sinus bradycardia sino atrial block, and heart block can usually be made at the bedside but electro cardiographic confirmation is ad vised In sinus bradycardia the pulse quickens gradually with effort atropine, or amyl nitrite, in sino atrial block and sometimes in 2 1 heart block the rate doubles abruptly, whilst in complete heart block the degree of acceleration is barely perceptible Heart block may also be recognised by study ing jugular pulsation and heart sounds (q v)

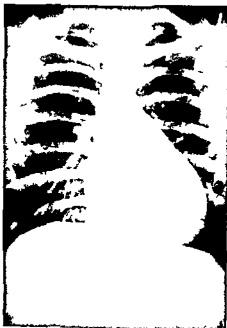


Fig 6 04—Relative cardiac enlargement due to sinus bradycardia

One of the consequences of sinus bradycardia is an increased ven tricular stroke volume of sufficient degree to maintain a normal cardiac output per minute When the heart rate is 40 the stroke volume approaches double the average normal the diastolic heart size is larger than usual (fig 6 04) and in time hypertrophy may occur Such enlargement is physiological

When the speed of the pace maker approaches 40 per minute it may become slower than the natural speed of impulse formation in the atrio ventricular node in which event nodal rhythm occurs As sinus arrhythmia is often associated with bradycardia it is more usual to see irregular examples of ventricular escape the A V node taking over whenever a pause is un usually long (fig 6 05) Nodal rhythm would supervene more frequently if the influences that retarded the sinus node did not also depress the A V node

Sinus bradycardia is often associated with sinus arrhythmia sometimes with auricular ectopic beats and rarely with paroxysmal auricular fibrillation or flutter in elderly subjects Vagal influences appear to be responsible

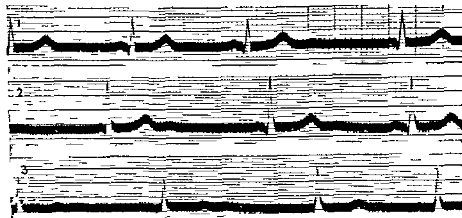


Fig 6 05—Nodal escape in sinus bradycard a

SINO ATRIAL BLOCK

There are three types of sino-atrial-block corresponding to similar varieties of A V block First beats may be dropped irregularly the pauses being roughly equal to two normal intervals (fig 6 06) like the dropped beats of partial A-V block with fixed prolonged P R interval Second beats may be dropped more or less regularly the pauses being always less than two normal intervals like partial A V block with progressive lengthening of the P R interval until conduction fails – the Wenckebach type Third there may be 2 1 sino atrial block every second beat being dropped this gives rise to a slow regular heart rate which doubles on effort or with atropine (fig 6 07) It should be understood that there is no electrocardio graphic representation of the formation and discharge of the excitatory

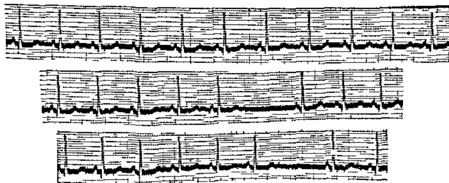


Fig 6 06—S no t ial blo k sho ng irregular dropped beats

impulse at the sinus node the first wave (P) of the electrocardiogram recording the passage of the impulse through the atria so that failure of conduction between the S A node and the atria can only be inferred

Sino atrial block is usually encountered in normal individuals, the first two types being commonly associated with sinus bradycardia It is a manifestation of increased vagal tone and may be abolished with atropine When there is 2 1 block and a pulse rate of about 40 per minute fluoroscopy may reveal cardiac enlargement due to the large stroke volume

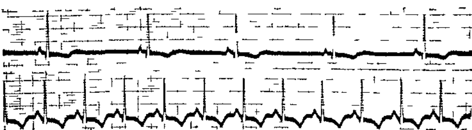


Fig 6 07—Sino atrial block the rate doubles on effort

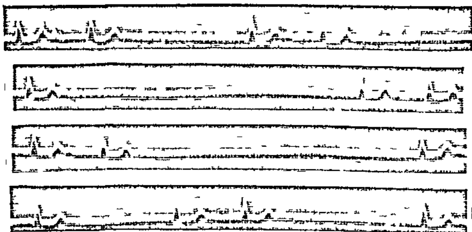


Fig 6 08—Cardiac standstill occurring spontaneously in sino atrial block (By c t sy f D Raymond D ley)

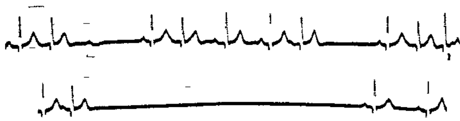


Fig 6 09—Cardiac standstill due to carotid sinus compression

necessary to maintain a normal cardiac output As with sinus bradycardia ventricular escape may occur and would probably be more common if the A V node were not also depressed

There are no symptoms of sino atrial block *per se* but occasionally short periods of cardiac standstill with dizziness or syncope may occur and appear to be due to bursts of extreme vagal activity (fig 6 08) They may be prevented by atropine Attacks of this kind may be readily induced in susceptible individuals by carotid sinus pressure (fig 6 09)

NODAL RHYTHM

The sinus node is the pace maker of the heart only because its inherent rate of impulse formation and discharge is quicker than that of any other focus endowed with a similar property but if it is sufficiently depressed as by cooling some other focus may form its impulses at a faster rate and so become the temporary pace maker, and in fact this function usually falls upon the atrio ventricular node Under such circumstances atrial excitation is retrograde and the electrocardiogram usually shows an inverted (or deformed) P wave just after the QRS complex and a heart rate of 40 to 60 per minute (fig 6 10a) Sometimes however the P wave may precede (fig 6 10b) or coincide with the QRS complex or it may be absent altogether owing to retrograde block (fig 6 10c) Occasionally it may shift its position from moment to moment (shifting or sliding nodal rhythm, fig 6 11) if such graphs are examined critically however they are seen to be examples of sinus bradycardia with normally formed P waves and frequent ventricular escape (so called wandering or shifting pace maker) This terminology is misleading for a wandering pace maker is simply dual rhythm both S A and A V nodes discharging spontaneously with variable asynchronism

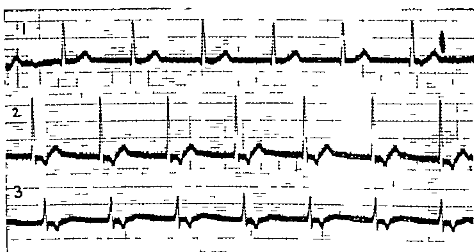
Clinically nodal rhythm may be recognised by its effect on the jugular venous pulse for whenever the right atrium contracts against a closed tricuspid valve sharp cannon waves occur (fig 6 12)

Nodal rhythm may be discovered by chance in healthy individuals it may occur in active rheumatic diphtheritic, and Fiedler s carditis, it may be momentarily induced by carotid sinus pressure and it may follow thrombosis of the right coronary artery above the origin of the branch to the sinus node (this branch arises from the left coronary artery in 40 per cent of cases) but its only common cause is digitalis therapy

Nodal rhythm is under autonomic control the heart rate being slowed by vagal stimulation and accelerated by atropine and exercise (White 1915) It is a harmless rhythm change gives rise to no symptoms and requires no treatment When due to digitalis, there is no need to stop the drug

Coronary sinus rhythm

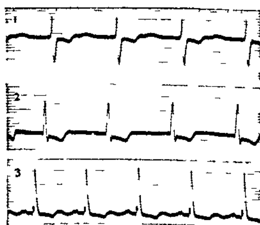
The position of the P wave in relation to QRS depends chiefly on the exact site of the pace maker in the A V node when situated in the proximal



(a) An inverted P wave occurs after QRS



(b) An inverted P wave precedes QRS (Coronary sinus rhythm)



(c)—The P wave is invisible possibly buried in QRS (leads 1 and 2 lead 3 shows normal rhythm)

Fig 6 10—Nodal rhythm

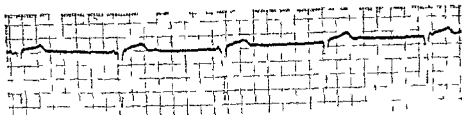


Fig 6 11—Asynchronous dual rhythm

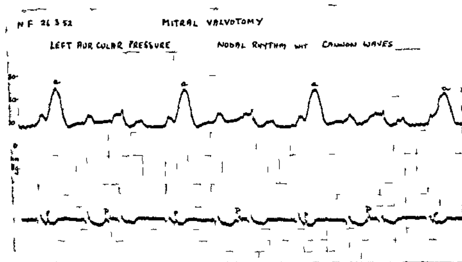


Fig 6 12 (a)—Nodal rhythm with partial retrograde block (Wenckebach type) showing reciprocal beats when the RP interval is sufficiently prolonged and cannon waves in the left atrial pressure pulse whenever the atria contract during ventricular systole

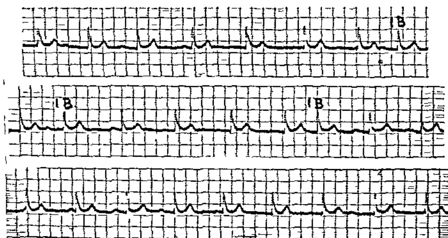


Fig 6 12 (b)—Interference dissociation The interference beats are labelled I B

or coronary sinus position of the node the pace maker is functionally nearer the atria than the ventricles and P falls just before QRS (fig 6 10b) This is called coronary sinus rhythm and is the most innocent and common type of nodal rhythm The P wave is nearly always inverted in standard leads II and III In view of the short P R interval the first heart sound may be accentuated

RECIPROCAL RHYTHM

When retrograde conduction to the atria is delayed in nodal rhythm the R P interval may exceed 0 2 second by then the ventricles may be no longer refractory and may be re activated by a return of the excitation wave from the atria so that a *reciprocal* beat as it is called follows the P wave A form of coupling known as *reciprocal rhythm* may be brought about in this way each pair of ventricular beats having an abnormal P wave between them (White 1921) or if retrograde R P conduction shows pro gressive lengthening reciprocal beats may occur only at intervals when R P is sufficiently prolonged (fig 6 12a)

INTERFERENCE DISSOCIATION

If retrograde conduction is completely blocked in nodal rhythm forward conduction remaining unimpaired *atrioventricular* dissociation occurs in which the ventricles beat faster than the atria the rate of discharge of the sinus node being necessarily slower than that of the A V node From time to time in such a rhythm atrial activation from the sinus node discharges the A V node prematurely and causes an *interference beat* the slightly irregular rhythm so produced being called *interference dissociation* (fig 6 12b)

HEART BLOCK

When any organic lesion or functional disturbance impedes conduction through the bundle of His or through both its main branches we may speak of heart block There are four grades prolonged P R interval dropped beats partial block with fixed atrio ventricular relationship and complete heart block

PROLONGED P R INTERVAL

As discussed elsewhere the upper limit of the normal P R interval should not exceed 0 22 second In partial heart block it frequently measures 0 28 to 0 32 second In extreme cases or when there is associated tachycardia electrocardiograms may show P coinciding with or even preceding the previous T wave (fig 6 13)

Prolongation of the P R interval may be transient or permanent or it may develop into a higher grade of block As a transient phenomenon it is especially characteristic of any form of active carditis but it may also be due to digitalis to coronary thrombosis, or to temporary nutritional

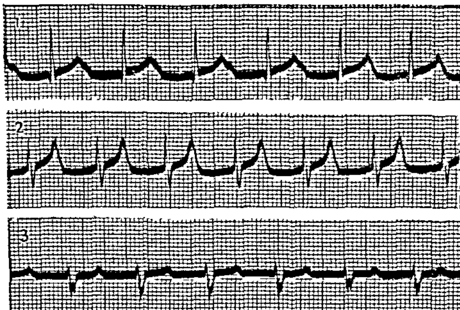


Fig 6 13—Prolonged P R interval with P coinciding with the previous T wave

changes from other causes and it may be induced by carotid sinus pressure Permanent delay in conduction may result from an inflammatory scar involving the bundle of His as in old rheumatic heart disease or from ischæmic fibrosis When the block is not permanent it may be relieved immediately by the intravenous injection of 1 to 3 mg of atropine sulphate (Bruenn 1937) A prolonged P R interval may also be shortened when the subject stands upright (Scherf and Dix 1952)

Although partial heart block of this kind is usually an electrocardio graphic diagnosis it may be recognised clinically by noting delay between

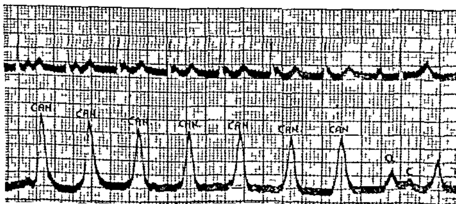


Fig 6 14—Partial heart block showing jugular cannon waves

the atrial and ventricular components of cervical venous pulsation or presystolic gallop rhythm by observing a gap between a presystolic murmur and the first heart sound in cases with mitral stenosis by hearing an unusually faint first heart sound or by detecting cannon waves in the neck when the P R interval is so prolonged that P falls between QRS and T in the previous cycle (fig 6 14) Its practical importance lies in its value as a sign of active rheumatic carditis

PARTIAL HEART BLOCK WITH DROPPED BEATS

In a slightly higher grade of partial heart block, conduction through the bundle of His fails *altogether* from time to time so that ventricular beats are dropped In the type first recognised by Wenckebach (1899) the P R interval shortens considerably after a beat is *dropped* but subsequently lengthens progressively *from cycle to cycle* until conduction again fails (fig 6 15) In another type (Hay 1906) the P R interval is fixed and beats are dropped irregularly and unpredictably

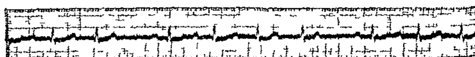


Fig 6 15—Partial heart block with dropped beats (Wenckebach type)

The condition may be detected clinically by noting a changing a c interval in the neck variations in the intensity of the first heart sound, and *occasional cannon waves (fig 6 14) It is commonly transient and recovers* spontaneously but occasionally progresses to complete heart block

PARTIAL HEART BLOCK WITH FIXED A V RELATIONSHIP

Relatively stable forms of partial heart block may be encountered, usually with a 2 1 atrio ventricular relationship (fig 6 16) but occasionally with

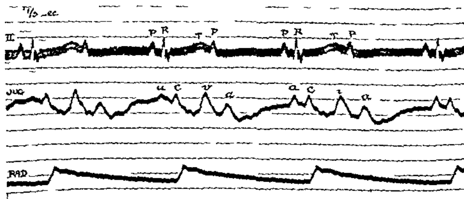


Fig 6 16—2-1 heart block
(By courtesy of Sir John Parkinson)

3 1 or even 4 1 A V ratios These usually progress to complete heart block they are much less common in active carditis than in ischæmic cases

Clinically 2 1 heart block has to be distinguished from sino atrial block from sinus bradycardia with a heart rate of about 40 beats per minute from nodal rhythm and from complete A V dissociation Failure to quicken appreciably with effort or atropine excludes sino atrial block and sinus bradycardia (and usually nodal rhythm) The absence of both irregular cannon waves and varying intensity of the first heart sound distinguish it from complete heart block

COMPLETE HEART BLOCK

Etiology Complete atrio ventricular dissociation is very rare in active rheumatic carditis but less so in diphtheritic carditis it may be induced by digitalis especially in cases of auricular fibrillation and has been caused by hæmorrhage into the bundle of His from trauma or asphyxia and by primary or secondary neoplasm About 10 per cent of cases are congenital (q v) As a rule however complete heart block is associated with ischæmic or hypertensive heart disease with syphilitic aortitis or with extensive calcification of the aortic cusps or mitral ring in elderly atherosclerotic subjects and is due to a fibrotic or calcified lesion in the bundle of His or in both its main branches Occasionally no cause can be found

Clinical features Complete A V dissociation is four times more common in males than in females and 84 per cent of cases occur in patients over 50 years of age (Campbell 1944) It is usually permanent but under special circumstances may be transient or even paroxysmal (Lawrence and Forbes 1944) It is characterised by an extremely slow heart rate a water hammer or collapsing pulse elevation of the venous pressure cervical venous pulsation unrelated to ventricular contraction audible independent atrial sounds the occurrence of cannon waves in the neck and varying intensity of the first heart sound general enlargement of the heart and syncopal attacks of a special kind It is proved electrocardiographically (fig 6 17)



Fig 6 17—Complete heart block Ventricular rate 18 beats per minute

Whilst the pulse rate is usually about 28 to 36 beats per minute based on the inherent rate of impulse formation of the idio ventricular pace maker distal to the block in the bundle of His it may be so slow as to induce a state of continual faintness (fig 6 18) as in the case originally described by Spens (1793) in which it fell to 9 beats per minute At the other extreme complete A-V dissociation may be seen with a ventricular rate of over 100 the ventricles sometimes beating more rapidly than the atria (fig 6 19)

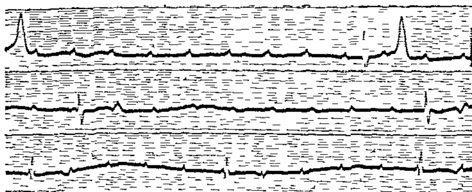


Fig 6 18—Complete heart block Ventricular rate 10 beats per minute

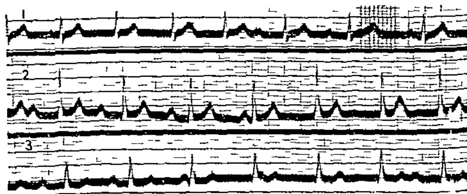


Fig 6 19—Complete A V dissociation with the ventricles beating faster than the atria

On the whole rates are faster when QRS is normal in width slower when the QRS resembles left or right bundle branch block (Kay 1948) Idio ventricular pace makers are little affected by stimuli that influence the S A and A V nodes so that the pulse rate usually remains remarkably constant in complete heart block In transient or paroxysmal cases how ever in which a functional element may be present temporary restoration of sinus rhythm may accompany fever as in the case described by Gerbezius in 1719 (Major, 1932)

A high systolic blood pressure is usual and is due to the large ventricular stroke volume Owing to associated vasodilatation however the pressure is not well maintained but tends to fall away rapidly in diastole giving rise to a collapsing pulse and to a rather low diastolic blood pressure

Under favourable circumstances inspection of cervical venous pulsation may reveal *atrial waves (a waves) independent of* ventricular events (c and v waves) as noted by Stokes (1846) Simultaneously may be heard the faint sounds of isolated atrial contractions (the semi beats of Stokes) either at the apex beat or down the left border of the sternum

Venous cannon waves occur when the P wave falls between QRS and T i e when the right atrium contracts against a closed tricuspid valve and are easily recognised by their abrupt quality high amplitude and variability Changing intensity of the first heart sound is equally characteristic the loudest sounds are heard when the P R interval is around 0 10 to 0 12 second left atrial contraction then forcing the mitral cusps wide open just before ventricular systole (Levine 1948) When the atria contract during *the period of rapid ventricular filling a loud third sound or short functional* mitral diastolic murmur may be heard the variability of this summation effect from beat to beat is as characteristic of complete heart block as the varying intensity of the first heart sound

Cardiac enlargement is usually more conspicuous than that seen in sino atrial block or in sinus bradycardia but is of the same quality unless the size and shape of the heart are altered by other effects of the underlying disease process

The cardiac output can only be maintained by a large stroke volume propelled with great force Diastolic distension is favoured by a compensatory rise in venous pressure and this must be very considerable during effort The early development of congestive failure is readily understood

Stokes Adams attacks Syncope due to ventricular asystole (Stokes Adams attacks) occurs in about 50 per cent of cases and is especially common when partial block becomes complete Loss of consciousness is abrupt without warning If standing the patient collapses and lies limp still pale and pulseless with fixed dilated pupils – as if dead breathing however continues If the attack lasts long enough i e for more than 10 seconds or so twitchings commence and may progress to convulsions and if ventricular asystole continues for more than 2 or 3 minutes recovery is rare As a rule however ventricular beating is resumed after a few seconds consciousness returns abruptly and a vivid flush ensues When an attack occurs in bed the lack of warning short duration of unconsciousness and abrupt return of full possession of the faculties may prevent a dull patient from being aware of the fit and he may only notice the flush The sequence of events both symptomatically and objectively is so characteristic as to make the diagnosis probable on the history alone – a point of some importance in patients with paroxysmal block who may present themselves with

normal sinus rhythm. In such [illegible] pressure may provoke an attack or induce paroxysmal [illegible]

Physiologically Stokes-Adams [illegible] to depression of a potential or established idioventricular [illegible] in cases of complete heart

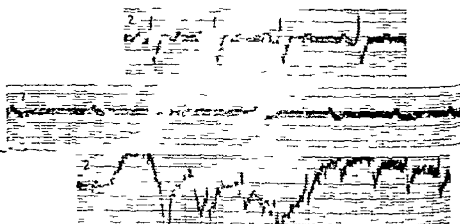


Fig. [illegible]—Stokes-Adams [illegible] induced by carotid sinus pressure in a patient with paroxysmal symptomless heart block

block the ventricles stand still while the atria continue to beat. They are apt to occur when *partial block* becomes complete either because such an event is usually associated with some depressive influence on conduction which may [illegible] depress ventricular pace-makers (even though considered beyond vagal control) or because idioventricular pace-makers are by nature initially sluggish. When complete block is well established attacks may still occur but are less common. The abrupt loss of consciousness depends upon sudden total failure of cardiac output. Twitching is due to cerebral anoxia and is not seen in short attacks. Convulsions are of two types one being an exaggeration of anoxic twitching, the other occurring after restoration of ventricular action and synchronising with the flush (*Formijne 1938*). In the second type convulsions and flushing appear to be due to carbon dioxide depletion in the blood stagnant in the lungs during the phase of asystole with continued respiration and to vasodilatation resulting from accumulation of tissue metabolites, so that when ventricular beating is resumed, blood rich in oxygen but containing practically no carbon dioxide is thrown abruptly into a widely dilated vascular bed. More often a period of apnœa follows the attack with or without subsequent Cheyne-Stokes breathing (Griffith 1921). Apnœa of course may also occur towards the end of long periods of ventricular asystole when it is due to failure of the respiratory centre resulting from profound cerebral anoxia.

An important complication of Stokes-Adams attacks is paroxysmal ventricular tachycardia or fibrillation (Parkinson, Papp and Evans 1941). In

such cases it may be impossible to determine clinically whether unconsciousness is due to asystole or to ventricular fibrillation It is probable that many deaths are due to the supervention of such rhythm changes rather than to asystole

Prognosis Congenital and transient cases do relatively well unless the disease responsible is serious for other reasons The outlook in paroxysmal and acquired permanent cases however is poor life expectancy averaging 4½ years (Graybiel and White 1936 Campbell 1944) Those with a history of Stokes Adams fits have a much worse prognosis than those without the majority of them dying suddenly Those without fits usually die from congestive heart failure

Treatment The most effective prophylactic treatment for faintness or syncope is the oral administration of ephedrine ½ grain (32 mg) t d s If attacks are frequent and the patient bedridden adrenalin, 0 5 mg (8 minims or 0 5 ml of a 1 1 000 solution) should be injected subcutaneously and repeated every two to six hours Sublingual isoprenaline 20 mg is also helpful (Nathanson and Miller 1949) but noradrenalin has very little stimulating action on ventricular rhythm (Nathanson and Miller 1950) Both ephedrine and adrenalin prevent undue depression of the ventricular pace maker and encourage the heart to beat a trifle faster It is sometimes said that idio ventricular rhythm cannot be influenced by any of the drugs or manœuvres that are known to affect the sinus node This is not always strictly true but changes are admittedly slight Effort for example may quicken the ventricular rate in complete heart block the adrenergic drug fever and even atropine may also do so In treatment however atropine is valueless alone although it may enhance the effect of adrenaline Barium chloride had a vogue its action depending upon its power to excite ventricular ectopic beats and so to prevent ventricular standstill but this is a poor substitute for the physiological benefit provided by ephedrine In paroxysmal cases when some functional disturbance must be postulated inhalations of amyl nitrite may abort attacks (Lawrence and Forbes 1944)

A problem arises when repeated seizures are partly due to paroxysmal ventricular tachycardia or fibrillation for if it is uncertain whether unconsciousness is due to asystole or to fibrillation the administration of adrenaline may be hazardous since the drug encourages the latter rhythm change If paroxysmal ventricular tachycardia is demonstrated neither quinidine nor procaine amide should be given for both depress conduction and may cause ventricular standstill (Miller *et al* 1952 Schwartz *et al* 1952 1953) Sublingual isoprenaline 20 mg has been recommended in these cases (Schumacher and Schmock 1954)

Very slow heart rates may be accelerated by means of intravenous infusions of sodium lactate in doses of 5 to 15 ml per minute of a molar (11 2 G per 100 ml) or half molar solution (Bellet Wesserman and Brody 1955) Lactate may serve as a myocardial fuel or the rise in pH (increased blood bicarbonate) that results from the treatment may accelerate the heart

Treatment of the primary cardiac condition may help This applies especially to the rare transient cases associated with active carditis or myocardial infarction and to permanent cases associated with syphilitic aortitis. Very rarely a small gumma may interrupt the conducting pathway, and the resulting block may be cured with iodides (Major, 1923)

If congestive heart failure calls for digitalis therapy the drug should not be withheld on account of coincident heart block but should be administered with caution Massive and intravenous doses should be avoided but digitalis leaf 3 grains (0 2 G) t d s on the first day 2 grains (0 13 G) t d s on the second and 1 grain (65 mg) thereafter twice daily is usually safe Should a Stokes Adams fit appear to be provoked the drug must be discontinued

In special clinics external electrical pace makers may be available to tide a heart over a critical period The machine is designed to deliver an electrical shock of 75 to 150 milliamps at 45 to 100 volts for two to three milliseconds 60 to 90 times per minute the negative electrode is placed over the region of the apex beat the positive on the opposite side of the chest posteriorly (Zoll Linenthal and Norman 1954)

BUNDLE BRANCH BLOCK

Although bundle branch block is not strictly a disorder of rhythm it may be discussed here conveniently on account of its close pathological relationship to other forms of conduction defect

Anatomy Bundle branch block occurs when some organic lesion interferes with conduction through one or other of the two main branches of the bundle of His As may be seen from figure 6 01 the main bundle after piercing the membranous septum divides into two, one branch passing down each side of the muscular interventricular septum just beneath the endocardium and spreading out fan wise distally the left branch may subdivide into anterior and posterior divisions in the lower half of the septum (Mahaim 1931) The A V node bundle of His and posterior division of the left bundle branch receive their blood supply from perforating septal arteries arising from the posterior descending branch of the right coronary artery, the right bundle branch and the anterior division of the left are supplied by perforating septal branches of the left anterior descending coronary artery (Gross 1921) Considerable variations occur, however, especially as vital reactions to ischæmia

Nomenclature When the left bundle branch is interrupted the excitatory process reaches the right ventricle first through the relatively normal right bundle branch and spreads throughout that chamber before passing across to the left The right ventricle therefore contracts first The electrocardiogram described and illustrated in Chapter III shows a wide QRS complex measuring from 0 11 to 0 18 second the main deflection of which is usually upright in lead 1 and downward in lead 3, with marked slurring or notching and followed by a conspicuous T wave usually in the opposite

direction Right bundle branch block (Wilson *et al* 1934) is characterised by widening of the initial ventricular deflection to 0 11 to 0 14 second by late slurring of QRS – usually best seen in S_1 – and by an upright T wave in lead I That the first type of graph described represents left bundle branch block has been proved by the reconstructed vectorcardiograms (monocardiograms) of Mann (1931) by the electrocardiographic discoveries of Wilson and his colleagues (1932) by kymographic and polygraphic studies revealing delayed left ventricular events (Wolferth and Margolies 1935) by experiments on revived human hearts in normal position in which one or other bundle branch has been cut (Kountz 1936) and by simultaneous electrocardiographic phonocardiographic and polygraphic records demonstrating and analysing ventricular asynchronism (Braun Menendez and Solari 1939) The detailed histological work of Mahaim (1931) which at first appeared to support the original view in which the nomenclature for left and right bundle branch block was reversed has been ably reviewed by Yater (1938) who presented extensive histopathological evidence of his own and concluded that the bilateral lesions invariably demonstrable rendered reliable interpretation difficult but that on the whole the findings supported the new terminology Finally the clinical facts cannot be disregarded left bundle branch block is commonly seen in lesions involving the left side of the heart whereas right bundle branch block is usually associated with enlargement of the right ventricle This general principle was recognised by Tung and Cheer (1933) and by Bayley (1934)

Etiology Left bundle branch block is usually due to hypertensive heart disease, ischæmic heart disease, or aortic valve disease right bundle branch block to mitral stenosis atrial septal defect or massive pulmonary embolism Either form may occur in active rheumatic diphtheritic or other form of carditis in any disease affecting the heart as a whole such as thyrotoxicosis and fibrosis of the myocardium of known or unknown etiology and as a result of any local lesion such as neoplasm Partial forms are common and tend to progress on the other hand both left and right bundle branch block may be transient paroxysmal or even alternating (fig 6 21) sometimes in association with paroxysmal tachycardia auricular flutter or fibrillation sometimes during an episode such as acute myocardial infarction congestive heart failure or massive pulmonary embolism but also spontaneously Right bundle branch block is sometimes found in otherwise healthy individuals even in youth left bundle branch block very rarely so

Clinical features Clinically left bundle branch block may be suggested by presystolic gallop rhythm in the absence of ventricular distress and by reversed splitting of the second heart sound A_2 falling after P_2 so that the split closes on inspiration and widens on expiration Right bundle branch block is suggested by wide splitting of the second sound P_2 falling later than usual When the heart is enlarged and it is uncertain which chamber

is mainly involved the presence of left or right bundle branch block points strongly to the homolateral ventricle Left bundle branch block provides convincing proof of serious heart disease but right bundle branch block must be interpreted more cautiously Neither form is influenced by digitalis atropine, or by any of the adrenergic or cholinergic drugs



Fig 6 21 – Alternating left bundle branch block

Prognosis The average life expectancy for cases of bundle branch block in general has been estimated at 3 years (Campbell 1944) but it should be clearly understood that in any given patient the prognosis is that of the underlying heart disease and is not influenced by the conduction defect Again if right bundle branch block is found in an otherwise normal individual the outlook does not differ from normal controls (Wood Jeffers and Wolferth 1935)

ECTOPIC BEATS

Ectopic beats are premature systoles induced by the discharge of some ectopic impulse forming focus situated anywhere in atrial nodal or ventricular tissue They are necessarily premature because all potential impulse forming foci are otherwise discharged by the excitation which reaches them from the sinus node

Physiology *In the atrial type* (fig 6 22) the P wave is abnormal in shape or direction according to the site of the ectopic focus and to the direction in which the impulse flows over the atria In these cases the partially charged sinus node is discharged when the impulse reaches it so that the compensatory pause following the ectopic beat is slight being equal to a normal cycle plus the interval between the onset of the ectopic and the

arrival of the retrograde excitatory process at the S A node The timing of the heart beat is permanently altered The ventricular complex is usually normal but may be slightly deformed as a result of a functional defect in conduction If an atrial ectopic beat is very premature it may be blocked altogether



Fig 6 2 —Atrial ectopic beats

Nodal ectopic beats (fig 6 23) are premature beats arising in any part of the atrio ventricular junctional tissue The QRS complex is normal or slightly deformed as described above but the P wave is inverted and occurs just before during or just after the QRS complex according to the more proximal or more distal site of the ectopic focus and to the degree of resistance opposed to retrograde conduction Discharge of the sinus node (unless there is retrograde block) again prevents a full compensatory pause

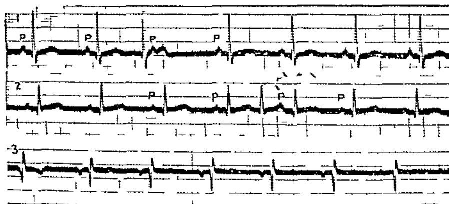


Fig 6 23—Nodal ectopic beats Slight deformity of QRS is due to fatigue block In I the P wave immediately after the ectopic is blocked In lead 2 the nodal ectopic is polated In both there is retrograde block

Ventricular ectopic beats are characterised by a full compensatory pause for the sinus node is not discharged by the premature impulse owing to retrograde block (physiological) in the bundle of His or to natural delay in retrograde conduction and so continues to function at its usual time Its first discharge after the ectopic however is blocked by the refractory state of the ventricles and so there is a pause until its second discharge The *final timing of the heart beat therefore remains unchanged* Electrocardiographically a ventricular ectopic beat resembles a bundle branch block

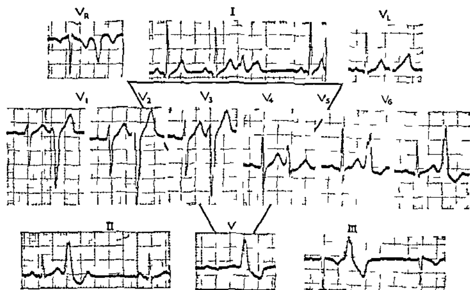


Fig 6 24—Right ventricular ectopic beats

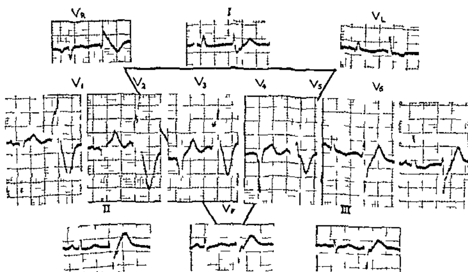


Fig 6 25—*Left ventricular ectopic beats causing coupling*

complex QRS being widened and notched and T being prominent and usually in the opposite direction When the deflection is like left bundle branch block the ectopic focus lies in the right ventricle (fig 6 24) when QRS is like right bundle branch block, the ectopic focus lies in the left ventricle (fig 6 25) There are many variations however depending upon the exact site of the irritable focus (Barker *et al* 1930 Kountz 1936) Ventricular ectopic beats may also be interpolated (fig 6 26)

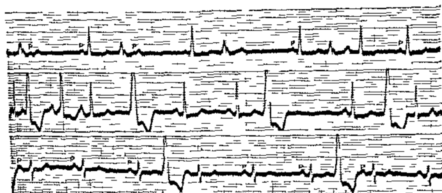


Fig 6 26—Interpolated ventricular ectopic beats

Premature beats have a smaller stroke volume than normal and if very premature may not be perceptible at the wrist or audible with a stethoscope The beat that follows is fuller than usual and is appreciated by the patient as a hard thump This is a matter of cardiac filling the earlier the ectopic beat the emptier the heart the longer the compensatory pause, the fuller the heart The blood pressure varies directly with the stroke output

Clinical diagnosis Clinically ectopic beats must be distinguished from other irregularities especially from auricular fibrillation and from partial heart block with dropped beats Whilst this may be easy in the majority of cases confusion arises with multiple atrial ectopic beats which may be indistinguishable from auricular fibrillation and with inaudible imperceptible or blocked ectopic beats which mimic partial heart block with dropped beats Alternate ectopic beats or coupled beats may be confused with S A block when very premature with a dicrotic or bisferiens pulse or even with pulsus alternans If there is any doubt the effect of effort amyl nitrite or of 1 mg of atropine sulphate should be determined ectopic beats usually disappear as the heart quickens, and may be exaggerated as it slows down again Ectopic beats often cause cannon waves in the neck whereas auricular fibrillation cannot do so

Etiology Experimentally ectopic beats may be produced by electrical stimulation of any part of the heart Certain drugs notably digitalis bari chloride and adrenaline may produce them Excessive use of tob

occasionally seems responsible They are common in pregnancy Whilst almost any state of ill health may be blamed for their occurrence no common factor has been discovered and in the majority of cases there is no evidence of structural disease of the cardiovascular or other systems Occasionally, however atrial ectopic beats may herald auricular fibrillation especially in mitral stenosis and thyrotoxicosis Under certain circumstances also ectopic beats are probably due to organic disease for example, their occurrence during the course of diphtheria may be due to toxic carditis but as innocent ectopic beats are common enough after simple streptococcal tonsillitis and indeed during convalescence from any fever it is impossible to draw any conclusion from their presence Again ectopic beats following coronary thrombosis are probably significant and to be explained by irritable foci set up by ischæmia but are equally common in conditions that may simulate myocardial infarction On the whole therefore it is wise to assume the innocence of ectopic beats under any conditions and to judge organic disease on other grounds

Treatment Many patients are unaware of premature systoles others may seek relief from palpitations Treatment includes fresh air exercise and a healthy physiological life Of drugs potassium bromide 10 grains (0 65 G) t d s phenobarbitone [1] grain (32 mg) t d s or quinidine 5 grains (0 32 G) t d s may prove effective Alternate ectopic beats (coupling) due to digitalis provide good grounds for stopping the drug or reducing its dose Potassium salts are efficient (Sampson and Anderson 1932 Castleden 1941) but the large dose usually required is not without danger of sudden death and may provoke symptoms as unpleasant as the palpitations chiefly nausea and vomiting the chloride or acetate is employed as a 10 to 20 per cent aqueous solution and may be given by mouth in safe doses of 2 to 4 G three or four times a day Larger doses are not advised Pronestyl 0 25 to 0 5 G four to six hourly by mouth usually abolishes ventricular ectopic beats Reassurance is important and should be unconditional and convincing for ectopic beats rarely constitute a complaint except in those prone to morbid anxiety

PARASYSTOLE

Parasystolic rhythm is said to occur when an ectopic focus releases an excitatory impulse at regular intervals independent of the pace maker The ventricles respond to this impulse whenever it reaches them outside their refractory phase

PAROXYSMAL TACHYCARDIA

When ectopic beats occur in rapid and regular succession from the same focus one may speak of paroxysmal tachycardia The name was introduced by Bouveret in 1889 The ectopic focus may be supraventricular (atrial or nodal) or ventricular The electrocardiographic complexes in the three types are precisely the same as those in the three types of ectopic beat

The patient usually complains of attacks of palpitations characterised by

the abruptness of their beginning and end by the rapidity and regularity of the beats and by the relative well being of the patient (Cotton 1867) Until an attack is witnessed the diagnosis rests upon an accurate history Experience shows that most careful cross examination is required to establish the true sequence of events It is not enough to determine that the onset is sudden it is necessary to be sure it is abrupt that the full velocity of the attack is reached immediately in the space of one beat that from no sensation whatever maximum palpitation develops within one second To assess the rate and rhythm it is helpful to ask the patient to represent them by tapping with his finger The manner in which the attack ends may be more difficult to establish some patients become accustomed to the palpitations and gradually fail to perceive them others pass from a true paroxysm to sinus tachycardia without appreciating the change and their description of the end refers to the gradual slowing down of the sinus rhythm

Attacks may last from a few seconds to several weeks but are usually measured in hours and rarely exceed three days The speed ranges between 110 and 250 beats per minute but is between 140 and 240 in 90 per cent of cases and between 150 and 200 in 50 per cent (Campbell 1947) Occasionally however much faster rates have been recorded For instance in one of Bouveret s cases the heart rate was 300 per minute If the heart is normal as it is in 62 per cent of the supraventricular variety, there is usually a remarkable degree of polyuria *during* the attack at least in cases with heart rates up to 180 beats per minute there are usually no other symptoms apart from those provoked by anxiety but if the attack is unduly prolonged or the heart rate exceptionally rapid congestive failure or angina pectoris may occur If the heart is abnormal however as it is in 80 per cent of the ventricular variety the rapid development of congestive heart failure is common With very rapid rates syncope may occur and in ischaemic heart disease status anginosus Physiologically, the effects depend upon the functional capacity of the heart to increase its output with tachycardia and on its ability to stand up to the extra work imposed with minimal rest In any given case there must be a critical rate above which the cardiac output falls

SUPRAVENTRICULAR PAROXYSMS

As just indicated both paroxysmal atrial and nodal tachycardia are most commonly encountered in healthy individuals and have little more significance than ectopic beats or spontaneous fluttering of somatic muscle They are fifteen times more common than ventricular paroxysms When attacks occur in patients with heart disease the prognosis is not so good and depends upon the nature and severity of the cardiac lesion and the speed and duration of the paroxysm Even so the mortality rate is only about 1 per cent

A clinical diagnosis may be accepted if the spontaneous or in

beginning or end of an attack is proved to be abrupt if the heart rate during a paroxysm exceeds 150 per minute and does not vary with effort, change of posture atropine amyl nitrite carotid sinus (or eyeball) pressure prostigmine, or mecholin if any such measure terminates the paroxysm if the duration of attacks is a matter of hours rather than one of minutes days or weeks if the patient is relatively young i e under 40 years of age or was so when he had his first attack if paroxysms have continued with variable frequency for more than five years and if there is no evidence of organic heart disease or thyrotoxicosis Electrocardiographic proof however which may require a record of the beginning or end of an attack should be obtained whenever possible Although only a rare chance will enable the onset to be registered the end may be recorded in over half the cases by means of a continuous tracing while the attack is terminated by carotid sinus pressure or mecholin (fig 6 27) If the attack is not terminated such measures may yet serve to differentiate paroxysmal tachycardia from sinus tachycardia and from auricular flutter for in paroxysmal tachycardia the heart rate is rarely altered whereas in sinus tachycardia it is slowed and in auricular flutter it is often abruptly halved Occasionally however carotid sinus pressure may block paroxysmal atrial tachycardia (fig 6 28)

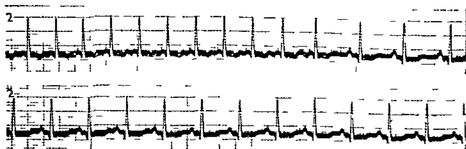


Fig 6 27—Paroxysmal atrial tachycardia terminated by means of mecholin

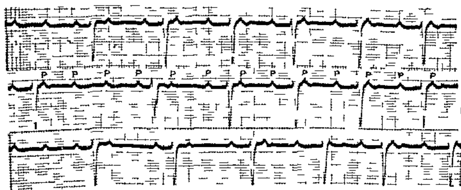


Fig 6 8—Paroxysmal atrial tachycardia blocked by carotid sinus compression

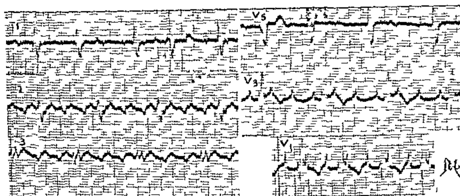


Fig 6 29—Paroxysmal atrial tachycardia showing varying degrees of spontaneous A V block



Fig 6 30—Paroxysmal atrial tachycardia slowed by means of quinidine

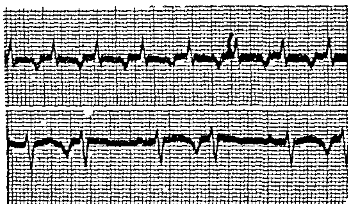


Fig 6 31—Paroxysmal atrial tachycardia followed by atrial ectopic beats

Evans (1944) first presented evidence based on lead CR1 suggesting that many cases that would ordinarily be interpreted as 2 : 1 atrial flutter might really be examples of paroxysmal atrial tachycardia with 2 : 1 A V block and that these two conditions were essentially the same Certainly paroxysmal atrial tachycardia may show varying degrees of A V block (figs 6 28 and 6 29) and the atrial waves may be slowed by means of quinidine (fig 6 30) in the same way as flutter there is also no doubt that the same patient may show all varieties of atrial rhythm suggesting that they all depend upon a similar mechanism and that the occurrence of atrial ectopics before or after a major attack (fig 6 31) offers an obvious clue as to their essential nature Indeed Prinzmetal (1950) has now provided convincing evidence not only of the unity of paroxysmal atrial tachycardia and flutter but also of atrial ectopic beats and auricular fibrillation all four disturbances of rhythm depending upon the presence and behaviour of an ectopic irritable focus Nevertheless the clinical differences between paroxysmal tachycardia and flutter (not to mention auricular fibrillation and ectopic beats) are considerable (Campbell 1945) and their separate identities should be preserved Similarly there can be no thought of not maintaining the separate identities of ventricular ectopics ventricular tachycardia and ventricular fibrillation yet all three must depend on a similar physiological mechanism

PAROXYSMAL NODAL TACHYCARDIA

Nodal paroxysms may be difficult to distinguish from atrial tachycardia when the rate is fast unless the beginning of an attack can be recorded (fig 6 32) At slower rates the electrocardiogram resembles fast nodal rhythm Clinically nodal tachycardia may often be recognised by the large regular cannon waves which dominate the jugular venous pulse (fig 6 33)

Nodal tachycardia is commonly innocent and responds particularly well to carotid sinus pressure and cholinergic drugs



Fig 6 3 —Paroxysmal nodal tachycardia beginning with a nodal ectopic beat

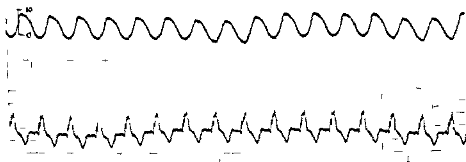


Fig 6 33—Paroxysmal nodal tachycardia showing regular cannon waves in the right atrial pressure pulse in a case of Ebstein s disease with right branch block

VENTRICULAR PAROXYSMS

Paroxysmal ventricular tachycardia is relatively rare is usually associated with organic heart disease in patients between the ages of 40 and 70 and is twice as common in men as in women It tends to arise in a badly damaged heart as in heart failure from hypertension or from aortic valve disease it may follow myocardial infarction or succeed a Stokes Adams fit occasionally it is due to digitalis in about 20 per cent of cases it is innocent

It has the same clinical features as the supraventricular variety apart from the circumstances in which it occurs and its lack of response to carotid sinus pressure and cholinergic drugs, moreover, it is more frequently followed by congestive heart failure and sometimes by ventricular fibrillation and sudden death The prognosis is correspondingly grave

Ventricular tachycardia may be recognised at the bedside if there are

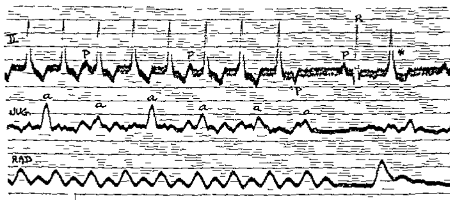


Fig 6 34—Paroxysmal ventricular tachycardia showing independent P waves at a slower rate Note the a wave and variable cannon waves in the jugular tracing

(B t sy f S J P rk n)

occasional cannon waves in the jugular pulse or if the first heart sound is occasionally extra loud, for both these phenomena indicate a varying atrio ventricular relationship

Proof of the nature of the attack is obtained by electrocardiography (fig 6 34) but difficulty may arise when supraventricular paroxysms or auricular flutter are complicated by previously established or functional bundle

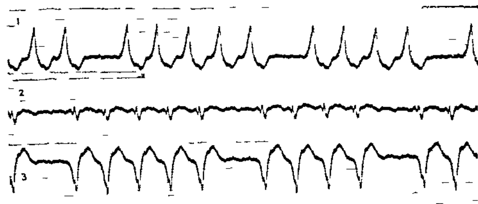
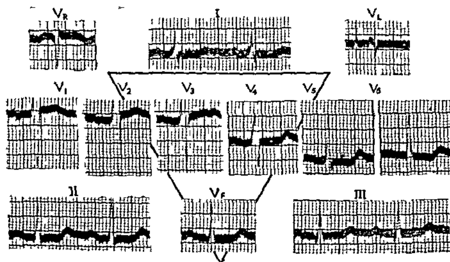


Fig 6 35—Auricular flutter with left bundle branch block

Fig 6 36—(a) During attack (rate 150)

(b) After resumption of normal rhythm showing inverted T waves over a wide area



(c) After normal rhythm has been maintained for three months

Fig. 6·36—Serial electrocardiograms from a case of paroxysmal ventricular tachycardia



(a) Acute cardiac dilatation



(b) Normal heart shadow after resumption of normal rhythm and recovery from congestive failure

Fig 6 37—Heart failure in primary paroxysmal tachycardia

branch block (fig 6 35) The diagnosis is more certain if independent P waves can be made out at a much slower rate but even then nodal tachycardia with bundle branch block and retrograde A V block is possible

Gross heart failure from prolonged paroxysmal ventricular tachycardia does not necessarily signify organic heart disease When the rhythm is restored to normal widespread inversion of the T wave points to nutritional changes in the myocardium but these are always reversible if the rhythm change is primary (fig 6 36) Cardiac enlargement due to failure is also reversible (fig 6 37)

TREATMENT

Supraventricular paroxysms *when of nodal origin* may be terminated by some mechanical trick already known to the patient such as holding the breath, by carotid sinus or eyeball pressure in about 50 per cent of cases and by the cholinergic drugs in 75 per cent Devices discovered by the patient include the adoption of some particular posture drinking iced water forced breathing or breath-holding compression of the abdomen and self induced vomiting

The carotid sinus is located at the bifurcation of the common carotid artery at the level of the superior border of the thyroid cartilage It should be firmly compressed for several seconds against the bodies of the cervical vertebræ by means of the observer s thumb first on one side then on the

other but never together Bilateral eyeball compression is also carried out with the thumbs should be sufficiently forceful to cause pain and should be maintained for 3 to 5 seconds A depressor response of the same kind may be elicited by stimulating the baroreceptors in both carotid sinuses and in the aortic bodies by injecting some pressor agent such as phenylephrine (neosynephrine) 0 25 to 0 5 mg intravenously (Youmans *et al* 1949)

Of the cholinergic drugs mecholin (acetyl beta methylcholine) is the most successful (Starr 1933) and prostigmine the least unpleasant in the doses employed doryl (carbo amino acetylcholine) is less effective and acetylcholine itself too drastic besides being technically difficult owing to its rapid destruction in the bloodstream Mecholin should be given intra muscularly or subcutaneously in a dose of 10 to 20 mg and may be expected to work in about five minutes prostigmine may be administered intravenously or intramuscularly in a dose of 1 to 2 mg and has its maxi mum effect in about half an hour Side effects include urgent micturition and defæcation colic vomiting sweating flushing and faintness but these are absent or slight with 1 to 1 5 mg of prostigmine and rarely severe with 10 mg of mecholin Should they prove too unpleasant and the object of the drug has not been achieved they may be abolished at once by injecting 1 to 2 mg of atropine sulphate intravenously but this is obviously not advised unless absolutely necessary Cholinergic drugs should not be given to patients who are prone to bronchial asthma for they may then excite violent bronchospasm

Paroxysmal atrial tachycardia does not usually respond to any of these measures the drug of choice in these cases being digitalis It was used originally to slow the ventricular rate by causing partial heart block as it does in flutter, and also to treat heart failure when that was present while these objects were being achieved normal rhythm was resumed so fre quently that digitalis had to be given the credit for that too For a quick response digoxin should be given intravenously in a dose of 1 0 to 1 25 mg and repeated in doses of 0 25 to 0 5 mg four to six hourly until some effect is observed or until 2 25 mg have been administered when subsequent doses must not exceed 0 25 mg Intravenous digoxin achieves its maximum effect in half to one hour if injections are given two hourly the dose should not exceed 0 25 mg after a total of 1 5 mg has been reached *An overdose of any digitalis preparation given intravenously may be fatal*

Ventricular paroxysms may be terminated by injecting intravenously 3 grains (0 2 G) of quinidine 0 2 to 1 G of procaine amide or 10 to 20 ml of a 20 per cent solution of magnesium sulphate (Boyd and Scherf 1943) Both quinidine in doses of 5 to 10 grains (0 3 to 0 6 G) and procaine amide 0 25 to 0 5 G may be given by mouth at two hourly intervals for four or five doses if the matter seems less urgent Armbrust and Levine (1950) found quinidine was successful when given by mouth in 81 per cent of cases—mostly ischæmic Procaine amide has a greater margin of safety than quinidine when given intravenously in the customary dose

The treatment of resistant cases of all forms of paroxysmal tachycardia may be very difficult It is essential first to establish the nature of the tachycardia beyond question a common error being to mistake supraventricular tachycardia with functional bundle branch block for ventricular tachycardia and hence to press home the wrong treatment Next heart failure must be treated vigorously if present, by all the usual remedies for when this is controlled normal rhythm may often be restored and maintained more easily Any underlying cardiovascular disease amenable to treatment such as hypertension thyrotoxicosis mitral stenosis and cor pulmonale should not be neglected Other contributory causes should also be recognised and dealt with if possible these include anxiety insomnia pregnancy alcohol bronchial carcinoma and other intrathoracic diseases If despite attention to such details the attack cannot be terminated or normal rhythm cannot be maintained for long the situation may be very serious Propyl thiouracil, starting with 300 mg daily, is worth trying Bilateral stellate and upper dorsal ganglionectomy abolished paroxysmal atrial tachycardia in several difficult cases reported by White and Bland (1950) but proved valueless in a case of the author s

When standard methods of treatment fail it is usually more profitable to review what has already been done in the hope of finding some fault in management that can be corrected than to resort to generally less effective methods of treatment such as syrup of ipecacuanha half an ounce (15 ml) as an emetic (Weiss and Sprague 1937) or atebrin 0 1 G intravenously 0 5 G in 10 ml of 1 per cent novocaine intramuscularly or 0 1 G three times daily orally (Gertler and Yohalem 1947)

Maintenance therapy

To prevent attacks of all kinds the best treatment is undoubtedly quinidine sulphate gr 3 to 15 (0 2 to 1 0 G) three times daily Heavy doses may not be tolerated but should be tried boldly if necessary (Gold 1950) Procaine amide 0 25 to 0 5 G three times daily, is also very useful particularly to prevent ventricular tachycardia A maintenance dose of digitalis may be best for atrial tachycardia and oral prostigmin 5 mg t d s if tolerated for nodal tachycardia

When attacks are infrequent short lived easily stopped and not disabling maintenance therapy is not advised for all the drugs mentioned may have undesirable effects on the patient s health and well being Procaine amide for example may cause agranulocytosis

PAROXYSMAL TACHYCARDIA ASSOCIATED WITH PRE EXCITATION

The condition first described as physiological bundle branch block with short P R interval (Wolff Parkinson and White 1930) is due to premature excitation of one or other ventricle usually the right resulting from an anomalous connexion between the A-V node or right atrium and the right

ventricle (Holzman and Scherf 1932) or to accelerated conduction of a portion of the excitatory process at the A V node (Prinzmetal *et al* 1952) probably the latter Electrocardiography shows widening of the QRS complex as in bundle branch block but at the expense of the P R interval which is shortened proportionally the P S interval as measured from the beginning of P to the end of the QRS complex remaining unchanged (fig 6 38) The appearances usually resemble left rather than right bundle branch block The anomalous pathway may be through the bundle of Kent (Wood Wolferth and Geckeler 1943 Kent 1914) or through abnormal conducting fibres arising from the upper part of the bundle of His (Wolferth and Wood 1933) such as those described by Mahaim (1931) The passage of the excitatory impulse down such an alternative pathway might well account for premature right ventricular stimulation Experimental short circuits of the kind envisaged were devised by Butterworth and Poindexter (1942) the classical appearances of the Wolff Parkinson White syndrome resulted On the other hand, Prinzmetal *et al* (1952) found that experimental W P W complexes produced by

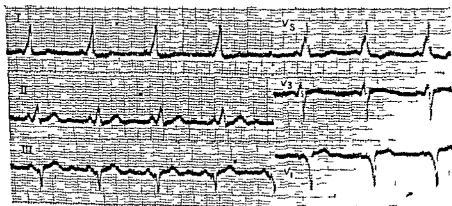


Fig 6 38—Pre excitation

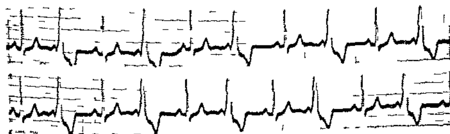
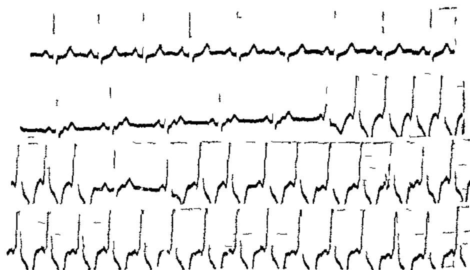


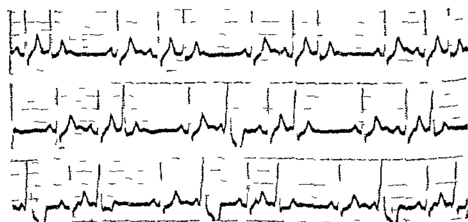
Fig 6 39 ... ng pre citation



(a)



(b)



(c)

Fig. 6.40—Wolff Parkinson White Syndrome showing
(a) Paroxysmal tachycardia with normal QRS complexes (b) Paroxysmal tachycardia with widened QRS complexes (c) Atrial re entry following the major attack

continuous subthreshold electrical stimulation of the A V node would not arise if the bundle of His was cut that W P W complexes sometimes occurred during cardiac catheterisation when the nodal tissue might be injured and after posterior cardiac infarction when the nodal tissue was proved to be injured at subsequent necropsy and that a ventricular form of W P W syndrome existed both clinically and experimentally in which pre excitation was due to an irritable focus in the ventricle Prinzmetal points out that one of the major functions of the A V node is to hold up the excitation wave sufficiently long to allow the atria to contract well ahead of the ventricles and that impairment of nodal function should therefore lead to accelerated conduction (Borduas *et al* 1955) Experimental damage to the A V node may certainly have this effect

The condition is usually congenital occurs in both sexes equally and is often unstable as shown by serial electrocardiograms indeed normal and abnormal complexes may alternate (fig 6 39) On the whole normal conduction is encouraged by atropine abnormal conduction by cholinergic activity (Duthie 1946) The heart is otherwise normal in at least 70 per cent of cases Pre excitation is clinically and academically important on account of its association with paroxysmal tachycardia, and is easily overlooked because casual electrocardiograms may be normal Paroxysmal tachycardia occurs in 50 to 70 per cent of cases (Willius and Carryer, 1946 Wolff 1954) and is often closely related to effort Electrocardiograms obtained during attacks suggest that their mechanism may depend upon a circus movement the impulse travelling down the bundle of His and back through the short circuit (fig 6 40a) or down the short circuit and back through the bundle of His (fig 6 40b) the former being more common Both types of paroxysm may occur in the same patient as in the illustrations In this particular case the second type of paroxysm was provoked by mecholin and before normal rhythm was resumed there was a period of transition in which abnormal P waves appeared immediately after certain QRS complexes (fig 6 40c) causing a single premature ventricular beat and suggesting circus movement due to retrograde conduction through the bundle of Kent or similar structure initial excitation having passed through the bundle of His Similar P waves may be seen in the upper half of figure 6 40b but these fail to excite the ventricles If Prinzmetal's hypothesis is correct paroxysmal tachycardia is presumably nodal and may be regarded as another manifestation of disordered nodal function Occasionally attacks resemble auricular flutter or fibrillation and the ventricular rate may be exceptionally fast A case described by Littmann nd Tarnower (1946) had an irregular ventricular rate of 340 per minute aroxysmal tachycardia may also occur in patients with a short P R nterval and without the W P W syndrome Thus Lows *et al* (1952) found in 9 5 per cent of 200 such cases When all cases with short P R interval nd paroxysmal tachycardia were considered only 18 per cent had the Volff Parkinson White syndrome

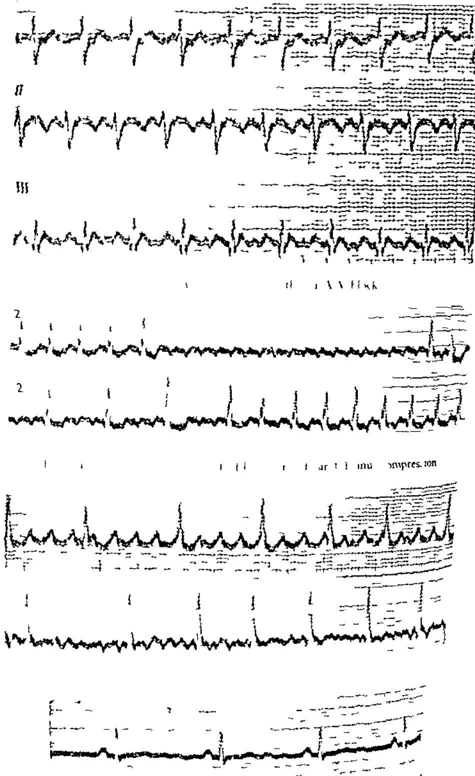


Fig. [illegible] Auricular flutter treated with digitalis. Auricular fibrillation induced; on withholding the drug normal rhythm is resumed

continuous subthreshold electrical stimulation of the A V node ... arise if the bundle of His was cut that W P W complexes ... occurred during cardiac catheterisation when the nodal ti sue ... injured and after posterior cardiac infarction when the nodal ti ... proved to be injured at subsequent necropsy and that a ventricul ... of W P W syndrome existed both clinically and experimentally in ... pre excitation was due to an irritable focus in the ventricle Prinzm... points out that one of the major functions of the A V node is to hold the excitation wave sufficiently long to allow the atria to contract well ahead of the ventricles and that impairment of nodal function should therefore lead to accelerated conduction (Borduas *et al* 1955) Experimental damage to the A-V node may certainly have this effect

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AURICULAR FLUTTER

Physiology Auricular flutter in man was so named by Jolly and Ritchie (1910) after obtaining the first electrocardiographic records of the condition and was attributed to a circus movement by Lewis (1918-20) The excitatory impulse was believed to travel round a ring of atrial tissue such as the mouths of the venæ cavæ as proved possible by the physiological researches of Mines (1913) Rosenblueth and Ramos (1947) apparently confirm Lewis views Using a high speed cinematograph technique however, Prinzmetal (1950) has disproved this thesis and has shown that auricular flutter and fibrillation like atrial ectopic beats and paroxysmal atrial tachycardia, depend upon the presence and behaviour of an irritable focus in atrial muscle The speed of the auricular beats ranges between 260 and 340 per minute and its rhythm is regular. As the A V node can rarely transmit impulses faster than 210 to 220 per minute, physiological heart block results the ventricles usually responding to every second impulse If the auricular rate is slower however and approaches 200 per minute as it may under the influence of quinidine the ventricles may be able to keep pace (Lewis 1925) If vagal tone is increased as by carotid sinus pressure a greater degree of physiological block results and an A V ratio of 4 1 or so may be established the speed of the f waves remaining unaltered Sometimes the ventricular response is irregular

Clinical features incidence and etiology Clinically flutter should be suspected in any patient presenting a regular heart rate of 120 to 170 per minute, uninfluenced by effort emotion or change of posture whether there are other indications of heart disease or not When the ventricular response is irregular the first heart sound varies in intensity according to the time relationship between atrial and ventricular contractions (Harvey and Levine 1948)

Flutter is a relatively uncommon but capricious rhythm and may occur when least expected It is twice as common in men as in women and its incidence increases with age being rare under 30 and most frequent (88 per cent) between the ages of 40 and 70 It is very rare in otherwise normal individuals it may complicate such diverse conditions as meningitis pneumonia cholecystitis or carcinoma of the colon In 90 per cent of cases however it is associated with organic heart disease especially rheumatic hypertensive ischæmic or pulmonary, and may then precipitate or complicate congestive heart failure According to Campbell (1947) angina pectoris develops in 25 per cent of paroxysms Attacks are commonly transient, and have the same abrupt onset as paroxysmal tachycardia but they tend to last longer, being measured in weeks rather than hours and may occasionally persist for years Lewis (1937) described a case in a parson which had continued for 24 years

Diagnosis is facilitated by carotid sinus pressure, which often causes abrupt temporary slowing of the ventricular rate as described previously whereas in sinus tachycardia slowing is commonly slight and in paroxysmal

tachycardia it is usually absent unless the attack is terminated Electrocardiography is advised in all suspected cases, however and reveals a continuous series of rapid regular atrial 'f' waves (fig 6 41) without intervening iso potential periods When there is 2 1 block, one f wave is more or less obscured by the QRS complex so that the nature of the

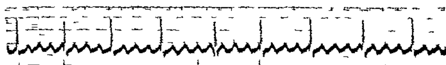
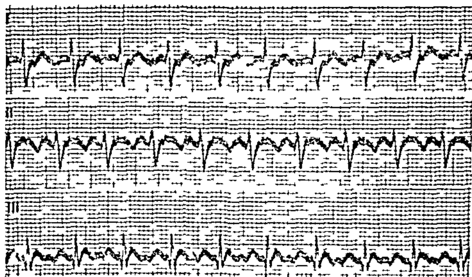


Fig 6 41—Auricular flutter with 4-1 A V block

tachycardia may remain uncertain (fig 6 42) Carotid sinus pressure aids analysis by increasing the degree of block and so unmasking such hidden f' waves (fig 6 43)

Treatment The patient should be put to bed and treated with adequate doses of digitalis, beginning with 8 grains (0 5 G) of the powdered leaf followed by 4 grains (0 25 G) and then by 2 grains (0 13 G) at six hourly intervals and continuing with 2 grains (0 13 G) t d s, until serial electrocardiograms show that auricular fibrillation has been established The drug is then withheld in the hope that normal rhythm may be resumed spontaneously (fig 6 44) Electrocardiographic control is necessary because the slow irregular ventricular response that results from such doses of digitalis is no proof of auricular fibrillation under the circumstances Adequate supervision is important owing to the heavy dose of digitalis usually required to induce fibrillation and if toxic symptoms appear dangerous before this result is achieved the attempt may have to be abandoned The effect of digitalis is twofold, as already indicated it encourages the irritable focus to assume the properties associated with auricular fibrillation and by depressing conduction in the bundle of His, it slows the ventricular rate. It was hitherto believed that normal rhythm was resumed when the circus movement was broken by the head of the wave meeting a refractory tail (Lewis 19 5) fo circus movement could not occur unless there was a gap of responsive tissue just ahead of the wave Digitalis, either during its administration or when it was suspended was thought to close the gap by having an unequal and favourable effect on conduction and on the refractory period Obviously, if conduction were quickened and the refractory period prolonged in atrial tissue the hypothetical gap would close Naturally no drug has this effect those quickening conduction also shortening the refractory period (like the cholinergic bodies) and vice versa (like quinidine) The action of digitalis is complicated by its cholinergic effect the f waves are never retarded, but they may be accelerated especially in those cases that are made to fibrillate (Wedd 1924)

Quinidine should not be given alone to cases of flutter in the first instance for by depressing the irritable focus and slowing the atrial rate, it may



Fi 6 42 – Auri ular flutt with r A V Bl k

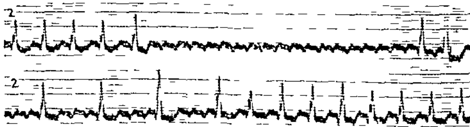


Fig 6 43—Aur ular flutt r larith 1 1 v 1 ar of carotid inus compre ion

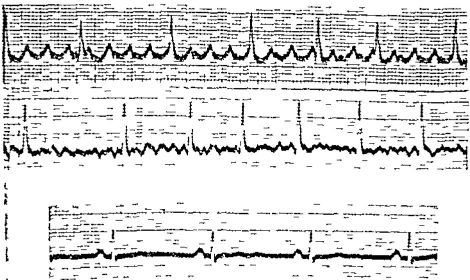


Fig 6 44—Auri ular flutter treated with di itali Auricular fibrillation is indu ed first on withholding the dru normal rhythm is re um d

allow the ventricles to keep pace rapid tachycardia resulting When auricular fibrillation has been established however the resumption of normal rhythm may be encouraged by quinidine in doses of 5 to 10 grains (0 3 to 0 65 G) two hourly to a maximum of 40 to 45 grains (2 5 to 3 G) in one day Quinidine may be given safely to resistant cases of flutter so long as the ventricular response is blocked by digitalis

If flutter continues despite all efforts to break it the patient should be kept on a maintenance dose of digitalis sufficient to control the ventricular rate but the result is rarely satisfactory for short of digitalis intoxication tachycardia due to 2 1 ventricular response is apt to develop on little provocation

In all cases attention should be paid to any associated disease cardiac or otherwise and to combating congestive heart failure

AURICULAR FIBRILLATION

Physiology According to Prinzmetal (1950 1952) two types of atrial contractions may be seen by means of a high speed cinematograph in experimental auricular fibrillation induced by means of aconitine or electrical stimulation (1) minute irregular contractions which he has called M contractions involving a small area of atrial wall (0 03 × 3 mm) and (2) large rhythmic wave like contractions (L contractions) which sweep across the atria 400 to 600 times per minute without pursuing a circus pathway Blocking a hypothetical circuit round the mouths of the venæ cavæ *had no effect on these waves Direct atrial leads recorded* by means of a cathode ray oscillograph showed very small M waves at *10 000 to 40 000 per minute and large f waves corresponding to the L* contractions The M waves did not occur in flutter Lewis s theory of circus movement appears to be untenable

At f wave speeds of 320 to 380 electrocardiograms from chest leads placed over the right atrium show f waves which at times are regular and even as in flutter and which at other times are irregular and uneven as in fibrillation (fig 6 45) At faster rates the f waves are always irregular in time and shape and the ventricular response is commonly rapid and chaotic varying between 100 and 200 per minute (fig 6 46) Sometimes and of course in treated cases when there is partial atrio ventricular block the ventricular rate is relatively slow Occasionally there is complete heart block (usually in cases treated with digitalis over a long period of time) and the ventricular rate is not only slow but regular (fig 6 47)

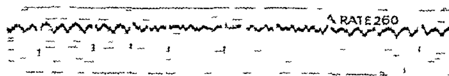


Fig 6 45 –Lead CR1 showing coarse auricular fibrillation or impure flutter

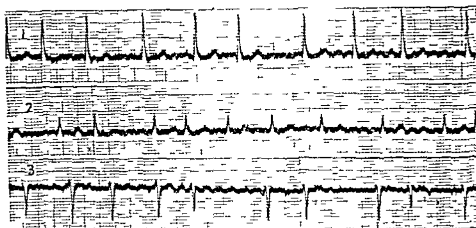


Fig 6 46—Auricular fibrillation

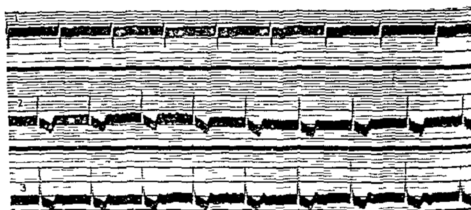


Fig 6 47—Auricular fibrillation with complete A V dissociation due to digitalis

The physiology of the circulation is disturbed by auricular fibrillation in several ways First the lack of atrial help deprives the heart of one of its reserves for powerful atrial contraction can increase the diastolic volume of the ventricles and so augment the force of their contraction second the ventricular rate is often fast enough to prevent proper cardiac filling so that the cardiac output falls—left ventricular filling is especially impaired with fast rates in mitral stenosis third the chaotic rhythm interferes with the mechanical efficiency of the heart many of the beats being wasted fourth the nutrition of the myocardium may suffer owing to reduced coronary flow Physiological studies have shown that when normal rhythm is restored the cardiac output rises immediately *even when the ventricular rate was previously controlled* by means of digitalis (Hansen *et al* 1952)

Etiology Auricular fibrillation is characteristically associated with mitral stenosis and toxic nodular goitre and is usually permanent with the former and paroxysmal with the latter It is not uncommon however in the later

stages of hypertensive and ischæmic heart disease On the other hand it is rare in congenital heart disease in bacterial endocarditis (2 per cent) in any form of active carditis in young people in aortic valve disease (unless there is stenosis of the coronary ostia) in pulmonary heart disease in the high output group (apart from thyrotoxicosis) and in pericarditis (although it occurs in 33 per cent of cases of Pick s disease) Like flutter more over auricular fibrillation may occur in patients with no other evidence of heart disease it may complicate head injuries meningitis pneumonia and other infections in rare instances, and it may even be found in apparently healthy persons The most important single factor determining the incidence of auricular fibrillation in those diseases that favour its occurrence is the advancing age of the patient

Clinical features Symptoms may be absent or negligible or the patient may complain of palpitations If the ventricular rate is very rapid syncope or angina pectoris may result as with flutter and paroxysmal tachycardia The mechanical inefficiency and nutritional hazards resulting from the rapid irregularity of the heart beat often lead to congestive failure when there is underlying heart disease on the other hand auricular fibrillation may be precipitated by congestive failure from other causes

Diagnosis The clinical diagnosis rests upon the recognition of a chaotic cardiac rhythm i e one without any semblance of order and must be distinguished from sinus arrhythmia, from ectopic beats, and from auricular flutter with an irregular ventricular response. Sinus arrhythmia should be recognised by its relation to respiration and ectopic beats by the perception of some fundamental order but multiple atrial ectopic beats may be most confusing The cervical venous pulse should be carefully inspected the presence of *a* waves cannon waves or a convincing v descent excludes auricular fibrillation Electrocardiography however is advised in all suspected cases

Treatment All cases in which the ventricular rate is accelerated should be treated with digitalis When there is no urgency a simple and safe method is to give powdered digitalis leaf, 3 grains (0 2 G) t d s on the first day 2 grains (0 13 G) t d s on the second and 1 grain (65 mg) t d s thereafter until the ventricular rate is controlled Subsequently a maintenance dose of 1 grain (65 mg) twice daily is usually sufficient When a quicker effect is desired the method described for cases of auricular flutter is advised If digoxin is preferred to digitalis folia equivalent doses may be used for the slow method of digitalising a patient and 1 5 mg 1 mg and 0 5 mg six hourly for the rapid method In urgent cases with very rapid ventricular rates and severe congestive heart failure digoxin by the intravenous route may be preferable, but is not without danger, and should never be given in full doses to any patient who may have had digitalis within the previous six weeks or who still shows a digitalis effect in the electrocardiogram The initial maximum dose is 1 5 mg , but 1 mg is safer and this may be followed by 0 5 mg and then by 0 25 mg at

intervals of not less than two hours and not more ... hours In favourable circumstances the ventricular rate may be ... within half an hour an oral maintenance dose should then ... intravenous doses just recommended Strophanthin may ... of digoxin as Ouabain it may be given in an initial dose ... intravenously, followed by 0 5 mg and then by 0 2 ... until the desired effect is obtained As strophanthin ... than forty eight hours it is preferable to digoxin ... effect is not desired

Other preparations of digitalis may be given ... dose being calculated according to the following table of ... th

Powdered digitalis leaf	[illegible]
Tincture of digitalis	10 m ...
Digoxin	0 ... m
Digitoxin (Nativelle's Digitaline)	0 ... mg

The practitioner is advised to become thoroughly familiar with a few reliable preparations Digoxin and digitoxin have the advantage of being pure crystalloids of fixed potency Digoxin is excreted more quickly than digitoxin The tincture loses strength with the passage of time and when mixed with other drugs and is therefore least reliable The powdered leaf has been the standard preparation in this country for many years but is being gradually displaced by digoxin

Toxic symptoms include anorexia nausea vomiting diarrhœa ectopic beats nodal rhythm heart block, paroxysmal tachycardia and sudden death from ventricular fibrillation Nausea and coupling due to ectopic beats are the best indications that the accumulated dose of digitalis is approaching dangerous concentration Unfortunately the worse the heart the closer the therapeutic dose becomes to the toxic the margin is never great The vagal effects may be relieved by atropine

The correct maintenance dose must be worked out for each individual receiving the drug but it averages 0 5 mg of digoxin daily ranging between 0 25 and 0 75 mg The average maintenance dose of digitoxin is 0 1 mg daily, and is very well tolerated by patients prone to nausea and vomiting because it does not irritate the gastric mucosa

Attempts to restore normal rhythm with quinidine should be made in all cases in which there is no evidence of intrinsic heart disease and especially in cases of successfully treated mitral stenosis or thyrotoxicosis also perhaps when auricular fibrillation is thought to have occurred prematurely or unexpectedly having been precipitated by some passing infection such as tonsillitis or pneumonia or by some other factor which either no longer operates such as pregnancy or which is itself controllable such as dental sepsis When fibrillation develops in the natural course of heart disease however, e g in cases of mitral valve disease which are unsuitable for

surgical treatment attempts to restore normal rhythm end in immediate or remote failure and should therefore be avoided as the procedure is not without risk

Quinidine should be given by mouth in doses of 5 grains (0 3 G) two hourly on the first day followed by 10 grains (0 6 G) two hourly on the second and by 15 grains (1 G) two hourly on the third to a maximum of 40 to 45 grains (3 G) per day the course being terminated immediately the rhythm returns to normal A maintenance dose of 5 grains (0 3 G) t d s is continued for a month in successful cases

Quinidine depresses the activity of the irritable focus, retarding its periodicity and often abolishing it altogether (about 75 per cent of cases) As the f waves slow down (fig 6 48) they may assume the regularity

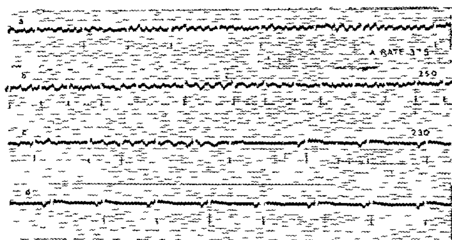


Fig 6 48—Auricular fibrillation treated with quinidine The f waves slow down from 375 to 230 per minute before normal rhythm is restored

of flutter and if their speed approaches 200 per minute there is danger of a 1 1 ventricular response. Tachycardia so provoked by quinidine may be prevented by preliminary digitalis therapy and a maintenance dose of digitalis is advised throughout the quinidine course The theoretical consideration that digitalis and quinidine have partly opposing actions does not prejudice successful practical results

Other complications of quinidine therapy include hypersensitivity and embolism Hypersensitivity may result in generalised œdema urticaria purpura fever vomiting and collapse although such symptoms are rare it is customary to give an initial trial dose of 3 grains (0 2 G) Less important symptoms of quinidine intolerance include epigastric pain nausea diarrhœa tinnitus and diplopia Quinidine lowers the peripheral vascular resistance and when given intravenously may cause syncope

To restore normal rhythm quinidine must usually reach a

concentration of 4 to 10 mgm per litre (Sokolow and Edgar 1950) The maximum blood level is achieved about two hours after an oral dose and then declines gradually over 12 to 24 hours The necessary blood concentration can be obtained when quinidine is given in the manner described above but Sokolow (1951) showed that it could also be reached with doses of 5 to 15 gr (0 3 to 1 G) t d s, the drug being cumulative for a period of three days Yount Rosenblum and McMillan (1952) agree with Sokolow that there are no contraindications to quinidine except hypersensitivity, and that there is no relation between inability to revert to normal rhythm and age, cardiac failure or *duration of fibrillation British schools are reserved* about accepting this conclusion

Important systemic emboli occur in about 5 per cent of all cases in which normal rhythm is restored and are due to the expulsion of left atrial thrombi There is reason to believe that only fresh thrombi are liable to be dislodged, and that these are most likely to form when the ventricular rate is rapid i e at the onset of the attack before digitalis has been given especially in cases of mitral stenosis when the left atrium and its append age are dilated Since normal rhythm is more likely to be resumed spon taneously or as a result of medical treatment at this time than at any other and since in fact systemic embolism is known to be a not uncommon complication of auricular fibrillation at this crucial time *whether normal rhythm is resumed or not* there are good grounds for treating all such cases with anti coagulants until the ventricular rate is properly controlled or normal rhythm is resumed and for withholding quinidine until the clotting mechanism has been depressed for at least five days—at any rate in cases of mitral valve disease Intracardiac thrombi are rare in thyrotoxic heart disease even under the most unfavourable circumstances owing to the rapid circulation associated with it

Lone auricular fibrillation also increasingly frequent as age advances may be paroxysmal or permanent In about 10 per cent of cases it causes congestive heart failure (Phillips and Levine 1949) and even in favourable cases it causes palpitations and reduces effort tolerance Since normal rhythm can be restored with very little risk in about 85 per cent for an average period of about two years in those that relapse and permanently *in 10 or 20 per cent of cases the general tendency* to treat conservatively with or without digitalis is open to criticism Heart failure when it occurs is reversible

Auricular fibrillation flutter and sinus bradycardia alternating in the same patient usually middle aged or elderly and otherwise normal can be very troublesome Short periods of cardiac standstill may result in syncope or very slow rates may give rise to weakness and dizziness when atrial flutter or fibrillation supervenes some patients actually feel better but complain of palpitations Treatment with atropine in the belief that both the abnormal atrial rhythm and the sinus bradycardia were due to increased vagal tone has proved disappointing

VENTRICULAR FIBRILLATION

Faradic stimulation of the ventricles invariably induces incoordinated fibrillation of the muscle which usually persists after cessation of the exciting cause The heart muscle is unable to expel its contents and syncope occurs abruptly Spontaneous recovery may occur especially in young healthy animals but sudden death is the rule When the heart is unduly excitable as in asphyxia digital pressure or gently scratching the surface

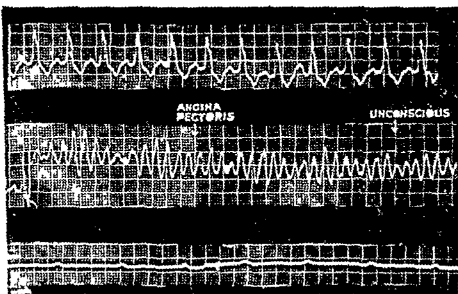


Fig 6 49—Ventricular fibrillation causing sudden death in a case of ischæmic heart disease

of the ventricle with a pin may be sufficient to induce ventricular fibrillation (MacWilliam 1887) Certain drugs may initiate the phenomenon notably adrenaline chloroform and digitalis Coronary occlusion is also known to be an exciting cause

Clinically ventricular fibrillation is often responsible for sudden death especially in ischæmic heart disease (fig 6 49) aortic stenosis syphilitic aortic incompetence diphtheritic carditis and complete heart block It also explains sudden death following intravenous injections of digitalis mercurial diuretics adrenaline and other drugs It is a rare complication of cardiac catheterisation and it occurs occasionally during or shortly after operations on the heart

Treatment is of little avail The intracardiac injection of quinidine sulphate 3 to 5 grains (0 2 to 0 3 G) or of 500 mg of pronestyl may be tried if circumstances are favourable Quinidine or pronestyl may also be given by mouth as a prophylactic agent when the risk of ventricular fibrillation is great A special electric defibrillator has been developed for surgical use and with cardiac massage may be life saving

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CHAPTER VII

HEART FAILURE

HEART failure has been defined as a condition in which the heart fails to discharge its contents adequately (Lewis 1933). The words may be applied logically to the heart as a whole or to one or other ventricle. The increased residual stroke volume of the failing human heart implied by Lewis' definition has been confirmed by modern work (e.g. Nylin 1943, 1945; Friedman 1950). Normally there are said to be about 99 ml of blood left in the right ventricle at the end of systole, the ratio $\frac{\text{residual volume}}{\text{stroke volume}}$ being around 1.75 (probably nearer 1.5); in advanced right ventricular failure the residual stroke volume may average as much as 500 ml and the ratio 13.6 (Bing *et al.* 1951).

Alternatively, heart failure may be defined as a state in which the heart fails to maintain an adequate circulation for the needs of the body despite a satisfactory venous filling pressure (the condition excludes extracardiac circulatory failure from hæmorrhage, vasovagal syncope or shock).

MECHANISM

The mechanism and even the definition of heart failure have been debated for over a century and are still a source of controversy. The back pressure theory, so well expressed by James Hope in 1832, which incorporates the idea of independent ventricular failure, maintains that when a ventricle fails to discharge its contents adequately, blood accumulates behind it and the pressure rises in the respective atrium and venous system. After holding sway for nearly a century this conception was replaced by the forward failure hypothesis of Mackenzie (1913), who believed that congestion depended upon failure of sufficient propulsion from behind, and who insisted that the heart failed as a whole. Before the second world war opinion reverted sharply to Hope's view, the arguments in its favour being well marshalled by Harrison (1935) and by Fishberg (1939); but the newer methods of investigation which provided much of the data upon which these arguments were based were crude, and subsequent technical refinements have disproved many of them. The introduction of cardiac catheterisation to the U.S.A. by Cournand and Ranges (1941) and to Great Britain by McMichael and Sharpey Schafer (1944) provided a new tool for studying the circulation in man, and modern hypotheses concerning the mechanism of heart failure have been much influenced by the pioneer work of these investigators (Cournand 1952; McMichael 1947, 1948).

The clinical facts are superficially simple enough. In predominantly

left sided lesions such as hypertension and aortic valve disease certain compensatory mechanisms are brought into play which help the left ventricle to shoulder its additional burden without embarrassing the organism as a whole Sooner or later and for one reason or another these adjustments no longer suffice and dyspnœa develops at first only on effort and then even at rest while orthopnœa and paroxysmal cardiac dyspnœa colour the clinical picture X rays show pulmonary venous congestion but the jugular venous pressure may be normal and there may be no œdema This syndrome is called *left ventricular failure* In purely right sided lesions such as primary pulmonary hypertension and isolated pulmonary stenosis the breakdown of compensatory adjustments (decompensation) results chiefly in fatigue elevation of the systemic venous pressure distension of the liver and dropsy while the lungs remain dry and radiologically clear This syndrome is called *right ventricular failure* Not infrequently cases of hypertensive heart disease or aortic valve disease start with left ventricular failure and later develop a rise of systemic venous pressure enlargement of the liver and dropsy this is called *congestive heart failure* A number of conditions that affect the heart as a whole such as isolated myocarditis may develop characteristic features of both left and right ventricular failure more or less simultaneously this too is called congestive heart failure In all the conditions so far mentioned there are usually signs of an impaired peripheral circulation as well due to a low cardiac output In the hyperkinetic circulatory states, however such as thyrotoxicosis anæmia arteriovenous fistula beri beri Paget s disease of bone advanced hepatic disease and anoxic cor pulmonale signs of congestive heart failure (both pulmonary and systemic) may be associated with warm hands throbbing digital vessels distended forearm veins and other evidence of an increased peripheral blood flow and raised cardiac output To distinguish these two types of failure McMichael introduced the terms low and high output failure The question at issue is just how all these manifestations of heart failure are brought about and what unifying principles underly them?

CARDIAC RESERVES

The terms compensation and decompensation are intended to define the physiological situation in respect of the cardiac reserves In compensated cases reserve mechanisms come into play which enable the diseased heart to carry on its prime function of maintaining an adequate circulation to all parts of the body without disturbing the function of any organ In mitral stenosis for example a rise of left atrial pressure may compensate for the obstruction but if this rise is too great pulmonary œdema interferes with the function of the lungs and endangers life even though the cardiac output is maintained Decompensation means that the heart can no longer maintain an adequate circulation for the needs of the body all reserves having been used At first this occurs only on effort (limited effort

tolerance) but finally even at rest (heart failure proper) To understand heart failure therefore it is necessary to know just what these reserves are and how they may break down

The strength of cardiac contraction

The most obvious way for the heart to meet an extra load would be for the muscle to contract more strongly in the manner of voluntary muscle It has long been known however that heart muscle always responds in precisely the same fashion to any strength of stimulus provided its intrinsic state is unaltered This is the all or none law (Bowditch 1871) It means that all fibres contract fully every heart beat so that at first sight there appears to be no room for a reserve mechanism here The proviso however is important for the intrinsic state of the muscle may well change not only from day to day but even from beat to beat There is good evidence for example that increased sympathetic tone augments the strength of cardiac contraction (Wiggers and Katz 1920) and that increased vagal tone weakens it (Peterson 1950) Stead Hickman and Warren (1947) believe that minor changes of cardiac output from minute to minute may well be a function of varying sympathetic tone Increased adrenergic activity may thus be regarded as the first reserve, and one that can be called upon almost instantaneously Artificial help of the same kind can be given by injecting adrenergic drugs

The strength of cardiac contraction must also be greatly influenced by any factor that alters or interferes with the natural biochemistry of heart muscle (Olson and Schwartz 1951) Digitalis may supply artificial bio chemical aid

Hypertrophy of the heart

Hypertrophy of the heart muscle is the natural long term method of increasing the strength of cardiac contraction Heart muscle fibres cannot multiply but they can increase in length and bulk This reserve is limited by nutritional difficulties for the nutritional needs of each muscle fibre depend on its cubic volume whereas its nutritional supply is proportional to its surface area thus as the fibre grows in volume there is an increasing disparity between demand and supply the former increasing by the cube the latter by the square Moreover the capillaries upon which the nutrition of the heart muscle depends do not increase as the heart hyper trophies (Katz 1954) Thus there may come a time when the heart is too big to be properly nourished

Increased filling pressure and cardiac dilatation

In 1884 Howell and Donaldson showed that the dog s heart increased its stroke output in response to an increased venous input More precisely the strength of cardiac contraction depended on the presystolic volume

and tension of the ventricles it was these which determined the magnitude of the all or none response (Frank 1895) In a series of papers Starling and his associates showed that the increase of stroke output that followed an increased filling pressure depended on the degree to which the ventricular muscle fibres were stretched at the end of diastole rather than upon the diastolic pressure itself also that a critical point was reached sooner or later beyond which further dilatation of the ventricles resulted in a fall of output (Starling 1918) In Starling s curve (fig 7 01) in which the cardiac

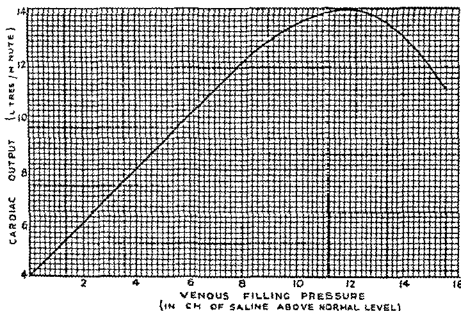


Fig 7 01—Relationship of cardiac output to venous filling pressure (Starling s curve)

output is plotted against the venous filling pressure (right atrial pressure minus the negative intrathoracic pressure) the ascent represents a compensated situation the descent a decompensated or overloaded state It is important to understand that the response of any particular heart to an increased filling pressure varies considerably according to the influence of other factors particularly those affecting the property of myocardial muscle fibres to stretch in response to a rise in diastolic tension (myocardial tone)

The venous pressure may rise primarily as a result of active or passive venoconstriction which reduces the capacity of the venous reservoir or because of an increase in blood volume secondary to sodium and water retention In either event the cardiac output rises and the elevated venous filling pressure is physiological (as on effort) compensatory (as in anaemia) or independent (as in acute nephritis) If the heart is flagging however and fails to empty itself properly its diastolic volume and pressure r

and the elevated venous pressure that results represents a state of de compensation This overloaded situation may be precipitated by an increase of blood volume resulting from sodium and water retention secondary to impairment of renal blood flow due to reduction of the cardiac output

A particular form of elevated venous filling pressure results from aug mented atrial systole A good example of this is seen in severe pulmonary hypertension or stenosis when powerful right atrial contraction causing a giant *a* wave in the venous pulse increases the diastolic stretch of the right ventricular muscle and so enhances the force of its contraction (fig 2 22)

The heart rate

If the venous filling pressure is maintained the cardiac output rises with increasing heart rates until a critical speed is reached beyond which the output falls rapidly (Henderson 1906) In man the critical rate is around 180, but varies greatly with the state of health of the heart When the venous filling pressure is maintained tachycardia increases the output because the major part of ventricular filling occurs early in diastole even at rates of 180 the ventricles may fill almost completely (Rushmer and Thal 1952)

It is not easy to investigate the effect of tachycardia alone on the cardiac output in man because other factors are difficult to keep constant for instance tachycardia produced by atropine usually results in a fall of venous filling pressure adrenalin cannot be used because it augments the force of cardiac contraction tachycardia produced by exercise is associated with a rise of venous filling pressure and with an increased force of cardiac contraction resulting from release of adrenergic tone

Certain observations on the effects of paroxysmal tachycardia are per tinent to this subject When the heart is healthy rates up to 180 are well tolerated and usually give rise to remarkable polyuria suggesting greatly increased renal filtration At rates between 200 and 250 polyuria is rare but angina breathlessness and fatigue are common At rates over 260 syncope is the rule Another point of importance is the duration of the tachycardia bouts lasting a few hours may have features suggesting a raised output such as polyuria hot extremities and distended forearm veins if the attack continues for several days however these signs may be replaced by those of a reduced output—vasoconstriction a rise of venous pressure oliguria œdema and fatigue suggesting that the nutrition of the myocardium has become impaired inversion of the T waves of the electro cardiogram after a prolonged attack confirms this supposition

In fact it has long been established that the benefits to be derived from tachycardia are limited by four factors (1) since the duration of systole varies with the square root of the cycle length diastole shortens dis proportionately as the rate increases until proper recovery can no longer take place (2) at rates above 180 diastole is so short that proper filling is

interfered with (3) as the rate increases the mechanical efficiency of the heart $\left(\frac{\text{work done}}{\text{oxygen consumed}}\right)$ declines (4) the coronary flow which is chiefly diastolic gradually becomes insufficient as the rate increases

Physiologically tachycardia is certainly used as a natural means of increasing the cardiac output and usually accompanies an increased filling pressure and greater adrenergic activity As a cardiac reserve in disease tachycardia is used especially in chronic constrictive pericarditis when it may be almost the sole means of raising the cardiac output and in the hyperkinetic circulatory states such as thyrotoxicosis anæmia and beri beri

HEART FAILURE

Of these four cardiac reserves the most important in relation to ordinary clinical heart failure is the combination of a raised venous filling pressure and dilatation of the ventricles hypertrophy is a long term matter autonomic influences of relatively fleeting importance and tachycardia rarely fast enough to be disadvantageous (except in paroxysmal tachycardia and uncontrolled atrial fibrillation) Heart failure means that the cardiac reserves no longer suffice to enable the heart to maintain an adequate circulation at rest and that increasing elevation of the venous pressure has distended the labouring ventricle beyond the point of critical diastolic stretch, so that further dilatation results in a fall in output

It is still not entirely clear just what causes the rise of venous pressure McMichael and Sharpey Schafer (1944) suggested that it might be a primary compensating mechanism presumably due to reflex veno constriction somehow excited by an inadequate output but there is no direct evidence in favour of this hypothesis There is no doubt that when a ventricle fails its diastolic pressure rises this must result in an increased pressure in the venous system behind the failing chamber There is also no doubt that heart failure results in diminution of renal filtration and total renal blood flow and that retention of sodium and water which is closely correlated with this increases the blood volume and causes œdema (Merrill 1946) the increased blood volume also raises the venous pressure Perhaps all three mechanisms come into play in greater or less degree

Forward failure

In the great majority of cases of heart failure the arterio venous oxygen difference is increased being over 50 ml per litre and the cardiac output reduced being less than 4 5 litres per minute at rest (Stead Warren and Brannon 1948) On effort the cardiac output does not rise but the arterio venous oxygen difference increases greatly (Hickam and Cargill 19

An exception to this general rule is the clinical syndrome of heart f (raised venous pressure hepatic enlargement and dropsy) associate

a raised cardiac output at rest which is found in anæmia beri beri, arterio venous fistula and other hyperkinetic circulatory states In these cases forward failure is relative

The effect of the lowered total output on the various territories of the body has been measured with reasonable accuracy

The cerebral circulation as might be expected is usually maintained at or near the normal level of 45 to 50 ml per 100 Gm per minute (Novack *et al* 1953)—about 0 8 litre per minute Disturbance of cerebral function in heart failure is therefore more likely to be due to hepatic or renal factors than to cerebral hypoxia

The renal blood flow normally about 1 3 to 1 5 litres per minute (Smith 1951) is notably reduced to about 0 5 litre per minute while the glomerular filtration rate declines from around 120 ml per minute to 70 or 80 ml per minute (Merrill and Cargill 1948) This is associated with salt and water retention an increased blood volume oliguria œdema and sometimes with a slight rise of blood urea The low renal blood flow is due to efferent *arteriolar constriction diuresis is always preceded by an increase of renal* blood flow which may be independent of any change in cardiac output and which occurs spontaneously at night (Brod and Fejfar 1950)

The total hepatic blood flow averages around 1 500 ml per minute (Bradley *et al* 1945) about 25 per cent of which is carried by the hepatic artery the rest by the portal vein In heart failure the flow is reduced in proportion to the reduction in cardiac output (Myers and Hickam 1948) and centrilobular necrosis is attributed to anoxia

The blood flow to the extremeties normally about 1 8 litres per minute (Abramson 1944) is reduced and further peripheral vasoconstriction occurs at once when patients are tilted head down even in left ventricular failure (Brigden and Sharpey Schafer 1950)

The coronary blood flow is said to be about 5 per cent of the cardiac output or around 75 ml per 100 Gm of heart muscle per minute i e 225 ml per minute for a 300 Gm heart Using the nitrous oxide method and coronary sinus catheterisation in man Bing *et al* (1949) found the normal left ventricular coronary blood flow averaged 65 ml per 100 Gm of left ventricular muscle per minute In congestive heart failure (from rheumatic heart disease) the coronary flow was much the same

Back pressure

Elevated ventricular diastolic pressure undoubtedly causes the rise in left atrial and pulmonary venous pressures in left ventricular failure Kopelman and Lee (1951) found that the intrathoracic blood volume was increased from an average normal of 1 8 litres to 2 7 litres All divisions of the lung volume are reduced except the residual air the total lung volume averaging about 1 5 litres less than the predicted normal (Richards *et al* 1951) The discrepancy between the two sets of figures may be due to an

increased amount of extravascular fluid in the lung parenchyma and lymphatics

Elevation of the right ventricular diastolic pressure (aided by an increased blood volume) raises the systemic venous pressure and distends the liver It is still uncertain to what secondary effects the raised venous pressure may give rise but it is not directly responsible for œdema

CAUSES OF HEART FAILURE

The heart may fail because it is overburdened by a raised ventricular pressure or by a raised cardiac output or because the health of the myocardium is impaired by inadequate or faulty nutrition metabolic disorder intoxication or intrinsic disease High outputs are tolerated better than high pressures but myocardial ill health is probably even more important Contributory factors include physical effort anxiety disturbances of rate or rhythm infection and pregnancy but all these are better expressed in more fundamental terms for example infection may increase the cardiac output and impair the health of the myocardium anxiety may raise the blood pressure in hypertensive heart disease and so forth Precipitating causes of this sort are found in 50 per cent of cases of heart failure (Sodeman and Burch 1938)

Viewing the subject in this way it should be clear that a high cardiac output is no more incompatible with heart failure than is hypertension that a heart capable of pumping ten litres of blood per minute is not necessarily better than one capable of maintaining a diastolic blood pressure of 140 mm of Hg Each is a measure of part of the total cardiac work performed neither alone is a sufficient measure of cardiac efficiency although their behaviour under certain experimental conditions may be Moreover the signs and symptoms of heart failure are largely due to alterations of pressure and volume in the pulmonary or systemic venous systems In left ventricular failure for example the redistribution of volume is the result of a short lived discrepancy between left and right ventricular outputs Although the balance must be restored quickly the consequences cannot be rectified until the process is reversed It should again be clear that such disturbances cannot be detected by casual estimations of the right ventricular output

LEFT VENTRICULAR FAILURE

When the left ventricle fails to discharge its contents adequately the pressure rises in the left atrium and pulmonary veins and blood accumulates in the pulmonary circulation

ETIOLOGY

Left ventricular failure may result from any disease which imposes an undue burden on the left ventricle or which interferes with its health These diseases include systemic hypertension from any cause aortic valve disease mitral incompetence myocardial infarction and a number of rare

cardiopathies which may affect mainly the left ventricle. In systemic hypertension the left ventricle may fail either because it is unable to meet the stress imposed upon it or because it is enlarged so greatly that it cannot obtain sufficient nourishment. As the nutritional demands of an individual muscle fibre depend upon its cubic volume and the nutritional supply is limited by its surface area there is an increasing disparity between the two as the muscle enlarges which sooner or later becomes critical (Gross and Spark 1937). In acute nephritis and malignant hypertension a rapid rise of blood pressure may cause left ventricular failure before there has been appreciable hypertrophy of muscle on the other hand in long standing cases of essential hypertension with gross enlargement of the left ventricle failure may occur even though the blood pressure has fallen to within normal limits failure then being attributed to nutritional break down In aortic valve disease in addition to these two factors there may be further interference with nutrition as a result of poor coronary filling due to a low mean blood pressure in aortic stenosis and to obstruction of *the mouths of the coronary vessels in syphilitic aortic incompetence* The cause of failure in uncomplicated ischaemic heart disease with myocardial infarction is due entirely to interference with ventricular nutrition resulting from coronary occlusion

PHYSIOLOGY

When the left ventricle fail to discharge its contents adequately its output falls its residual stroke volume increases its diastolic pressure rises and the pulmonary venous pressure rises if the right ventricle is healthy it continues to pump its normal quota and within a few minutes the total blood volume is redistributed more being held in the lungs and less in the greater circulation than before. With increased diastolic stretch the left ventricle may be able to cope with the situation and the balance between ventricular outputs is restored In other words in pure left ventricular failure the cardiac output is at first maintained at the expense of a dilated left ventricle a raised pulmonary venous pressure and an increased quantity of blood in the lungs Symptoms are due to pulmonary venous congestion and in a sense this is still a compensated state although a none too happy one If the left ventricle becomes overloaded any further rise of pulmonary venous pressure results in a fall of left ventricular output and a vicious circle is established Several things may prevent disaster (1) a high pulmonary venous pressure passively raises the pulmonary artery pressure and so loads the right ventricle (2) sometimes active pulmonary vasoconstriction adds greatly to this load (3) the redistribution of the blood volume may lower the right ventricular output which can only pump what it receives (4) bulging of the interventricular septum into the cavity of the right ventricle may reduce the diastolic capacity of that chamber (Bernheim effect) and (5) the pericardium which tends to limit ventricular distension must exert some increased pressure

on the right ventricle if greatly stretched by enlargement of the left If the pulmonary venous pressure rises beyond 35 mm Hg the patient is in danger of losing his life from pulmonary œdema

CLINICAL FEATURES

The symptoms of left ventricular failure are undue breathlessness on effort orthopnœa paroxysmal cardiac dyspnœa and acute pulmonary œdema The findings include bilateral basal pulmonary rales radiological evidence of pulmonary congestion and hydrothorax diminution of all fractions of the lung volume except the residual air an increased quantity of blood in the lungs increased intrapleural respiratory pressure swings a raised left atrial pressure with steep y descent and prolongation of the pulmonary circulation time The diagnosis is supported by gallop rhythm pulsus alternans and Cheyne Stokes breathing and is confirmed by the *demonstration of a suitable cardiovascular disease e g systemic hyper* tension aortic valve disease mitral incompetence or myocardial infarction

Undue breathlessness on effort Breathlessness due to left ventricular failure depends upon pulmonary venous congestion which both reduces ventilation and increases the work of breathing (Christie and Meakins 1934) It is not due to anoxia to an increased CO_2 tension or to a fall in pH

Orthopnœa paroxysmal cardiac dyspnœa and pulmonary œdema As these three conditions depend on variations of the same fundamental mechanism they are considered together When a patient adopts the upright or sitting position in order to breathe comfortably he may be said to have *orthopnœa* Although an almost constant sign of left ventricular failure it is by no means pathognomonic for it may be found in severe mitral stenosis bronchial asthma and in pericardial effusion The vital capacity is reduced in all these conditions and is greater in the upright than in the horizontal position but its relationship to orthopnœa is not necessarily direct More over its increase in the erect position is greater than can be explained by descent of the diaphragm The discrepancy is due to concomitant changes in the pulmonary circulation the amount of blood in the lungs being greater perhaps by as much as 500 ml in the horizontal than in the erect position (McMichael 1939) The redistribution of blood depends upon the geographical relationship of the atria to their respective venous systems As the right atrium is nearer the head than the feet the pressure within it rises when the body is tilted head down owing to the influence of gravity The right ventricle responds according to Starling s law and pumps more blood into the lungs in the horizontal than in the vertical position (McMichael 1937) The pressure within the left atrium however which is situated more or less in the centre of the lungs is not directly influenced by gravity and the left ventricular output does not therefore immediately keep pace with the right Only when the left atrial pressure rises propor tionately owing to an increased volume of blood in the pulmonary venous system will the balance be restored As patients with left ventricular failure

already have pulmonary congestion the extra engorgement which results from adopting the horizontal position may prove critical moreover if the left ventricle is already overloaded it will not respond to the rise in the left atrial pressure but will fail the more

Paroxysmal cardiac dyspnœa usually occurs at night The patient awakes with a feeling of suffocation and sits bolt upright gasping for breath he may climb out of bed and open a window or walk about in an agitated way

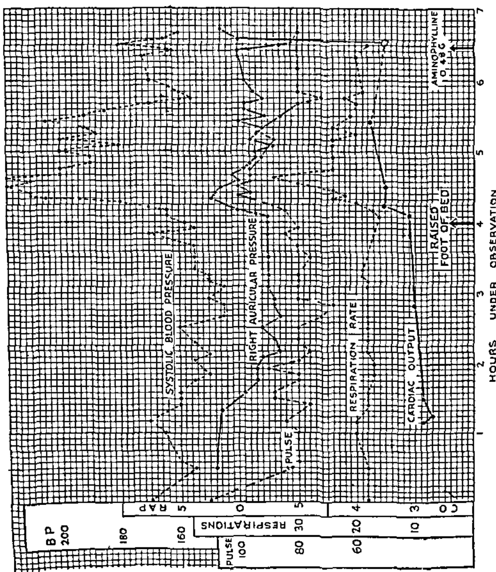


Fig 70 —Graph illustrating typical changes in blood pressure right auricular pressure pulse rate respiration rate and cardiac output in an attack of paroxysmal cardiac dyspnœa initiated in a patient with left ventricular failure by raising the foot of the bed The effect of aminophylline is shown at the end

In cases of simple orthopnœa this behaviour brings immediate relief but in paroxysmal cardiac dyspnœa the feeling of suffocation increases and the struggle for breath lasts for ten to twenty minutes Coughing and wheezing are commonly associated (*cardiac asthma*) and the patient may complain of palpitations faintness or substernal tightness The skin is pale cyanosed and cold indicating profound vasoconstriction and sweating may be profuse The blood pressure and venous pressure are both raised Attacks usually subside spontaneously but may be repeated nightly or at intervals of days or weeks In more severe cases *pulmonary œdema* develops Widespread crepitations are then heard over the lungs and quantities of frothy pink or white watery fluid are expectorated

Such attacks may sometimes be provoked by effort or by a rigor They are easily induced experimentally in susceptible subjects by raising either the venous pressure or the blood pressure by artificial means (fig 7 02) The mechanism probably depends upon acute discrepancy between right and left ventricular outputs, so that both the pressure and volume of blood in the pulmonary circulation reach critical levels Measurements of pressure changes by means of an indwelling cardiac catheter in spontaneous nocturnal attacks indicate that the venous pressure may rise before the blood pressure When attacks are induced by raising the venous pressure the cardiac output may rise Thus although the heart is said to be failing it may in fact be performing more work than usual both with respect to blood pressure and output The laboured breathing may be due in part to the extra effort required to inflate and deflate a turgid lung the intrapleural pressure showing greatly increased fluctuations (Heyer *et al* 1948) In frank pulmonary œdema however ventilation is seriously impaired and dyspnœa is partly due to anoxia

Certain difficulties in our understanding of these attacks must be faced It is by no means clear just why they occur at night or during sleep it has been suggested that depression of the nervous system during sleep allows too great a degree of pulmonary venous congestion to take place before hyperventilation wakes the patient and forces him to lower the right ventricular output by adopting a more upright posture so that relief comes too late to prevent a major attack also that reabsorption into the blood stream of tissue fluid formed during the daytime owing to disturbed renal physiology results in a rise of blood volume and venous pressure which augment right ventricular output and so increase pulmonary venous congestion (Perera and Berliner 1943) But the physical inactivity and muscular relaxation during sleep lower the systemic venous pressure by providing a larger effective venous reservoir and this should help to relieve pulmonary venous congestion again reabsorption of tissue fluid is due to the spontaneous diuresis that takes place during the night in cases of heart failure an event which should also relieve pulmonary venous congestion According to Brod and Fejfar (1950) the increased renal blood flow responsible for nocturnal diuresis is independent of any change in

cardiac output or right atrial pressure Another difficulty is the variable relationship between left atrial pressure and transudation of fluid from the pulmonary capillaries into the alveoli theoretically this should occur whenever the left atrial pressure exceeds the osmotic pressure of the plasma (about 30 mm Hg) but in practice much higher hydrostatic pressures may be recorded in the pulmonary capillaries without pulmonary œdema developing The state of the connective tissue between the alveolar membrane and the capillary may partly explain this for if collagen is much increased here it may serve as a barrier which tends to prevent fluid passing from the capillaries into the alveolar spaces (Hayward 1955) The efficiency of the pulmonary lymphatics in removing protein containing fluid from the walls of the alveoli must also be important Capillary permeability is increased by infection and by anoxia (Maurer 1940) both of which may encourage pulmonary œdema The high protein content of pulmonary œdema fluid (2 to 4 per cent) certainly proves that the capillaries are allowing much protein to escape during the attack (Drinker 1945), and this must greatly reduce the differential osmotic pressure across the capillary membrane Then the part played by bronchospasm must not be overlooked This is a variable complicating factor which increases ventilatory difficulty and the labour of breathing encourages hypoxia and favours the small hours it occurs in about half the cases and is presumably a reaction to congested bronchial mucosa Finally it is by no means clear why the attacks usually terminate spontaneously The great respiratory struggle the mental anguish that goes with it the increasing anoxia and bronchospasm all tend directly or indirectly to encourage the transudate only the natural adoption of the upright position works in the right direction Since acute hypoxia causes pulmonary vasoconstriction (Liljestrand 1948) active pulmonary hypertension might be expected to terminate the attack by reducing the output of the right ventricle but there is no evidence so far that acute pulmonary œdema increases the pulmonary vascular resistance

Bilateral basal pulmonary rales and hydrothorax Basal rales diminished air entry into the lower lobes and some impairment of the percussion note at the bases are said to be usual in left ventricular failure but in the author s experience such auscultatory signs are more likely to be absent or misleading Crepitations when due to pulmonary œdema are widespread rather than basal, and when there is no pulmonary œdema râles can only be bronchial *A raised pulmonary venous pressure per se gives rise to no auscultatory signs whatever* If the bronchial mucosa is congested bronchial secretions may be excessive or there may be broncho spasm but these bronchial rales and rhonci are inconstant and unreliable signs of left ventricular failure and are much more commonly due to chronic bronchitis Thus the oft repeated comment concerning the discrepancy between the site of pulmonary venous congestion as viewed radiologically when it is perihilar, and as heard clinically when it is basal is explained by the

simple fact that what is heard is not pulmonary venous congestion Bedford and Lovibond (1941) found that hydrothorax was a common complication of pulmonary congestion from left ventricular failure and that although often bilateral, tended to be more marked on the left side Its occurrence may depend upon the fact that the visceral pleura is drained by the pulmonary rather than by the bronchial veins (Miller 1937) but its precise mechanism is not yet fully understood

Radiological signs of pulmonary congestion The increased opacity seen in skiagrams is hilar and probably due to chronic interstitial œdema (fig 7 03) During attacks of acute pulmonary œdema a fleecy mottling spreads out from the hilum on both sides (figs 7 04 and 7 05) Hydrothorax may also be revealed by X rays perhaps when unsuspected clinically Interlobar effusion may be responsible for a rounded transient sometimes migratory opacity—the so called vanishing tumour of the lung Confirmatory evidence of left ventricular failure may be obtained by noting the size and shape of the heart shadow

Reduction of the vital capacity and lung volume The vital capacity is reduced by an amount equivalent to the extra quantity of blood and interstitial fluid in the lungs it is reduced much more if there is pulmonary œdema or a large hydrothorax as well and by a further few hundred ml according to the degree of cardiac enlargement Readings of 1 000 to 1 500 ml are common and may be as low as 500 ml when there is pulmonary œdema or hydrothorax



Fig 7 03—Pulmonary congestion in left ventricular failure (case of syphilitic aortic incompetence)

The lung volume is reduced proportionately the residual air remaining unchanged This at once distinguishes the condition from emphysema in which a low vital capacity is associated with a normal lung volume and increased residual air

As stated previously intrapleural respiratory pressure swings are excessive owing to increased resistance on the part of the turgid lung to both inflation and deflation

Prolongation of the pulmonary circulation time The normal arm to tongue

circulation time as measured by decholin or saccharin (q v) averages 13 5 seconds, ranging between 9 and 18 seconds Since the time taken by the substance to travel from the left ventricle to the tongue may be neglected and the journey from the antecubital vein to the right atrium takes only two or three seconds (Blumgart and Weiss 1927) the total arm-to tongue time is governed chiefly by passage through the lungs Using



Fig 7 04—Acute pulmonary œdema from left ventricular failure



Fig 7 05—Acute pulmonary œdema in mitral stenosis

(Acknowledgment to Dr G Graham Hayward)

radium C intravenously, which can be detected at any given point in the circulation by means of a special radio sensitive instrument, Blumgart and Weiss also showed that when the systemic venous pressure is raised in congestive heart failure the delay between the antecubital vein and the right atrium does not exceed five seconds even in gross cases It follows that with pure right ventricular failure the arm to tongue circulation time should not exceed 23 seconds and should often be within normal limits in fact this is so On the other hand in left ventricular failure the average time is 30 seconds (Wood 1936) and may be much longer The delay is due to pulmonary congestion and occurs presumably on the venous side

The arm to lung time The arm to lung time as measured by ether or amyl acetate (q v) is said to be helpful in distinguishing primary left from pure right ventricular failure if the total arm to tongue time is also known When the delay is proximal to the heart as in pure right ventricular failure the arm to lung time is delayed as much as the arm to tongue time on the other hand if there is further delay in the pulmonary veins as in primary left ventricular failure the arm to tongue time is disproportionately prolonged Although theoretically this test might seem helpful in fact

it is rarely so for two reasons first because the end point in the lung both with ether and amyl acetate is often unreliable and indefinite and second because it is easier and no less accurate to allow 1 to 5 seconds for delay proximal to the heart according to the degree of systemic venous engorgement'

Raised left atrial pressure with steep y descent

Cardiac catheterisation in cases of left ventricular failure has revealed mean indirect left atrial pressures in the expected range between 10 and 30 mm Hg above the sternal angle Unlike the tracings in mitral stenosis however the pressure drops rapidly after the opening of the mitral valve the down stroke of z or the y descent being remarkably steep the trough y may be followed by a fairly sharp rise of pressure back to the z point (fig 706) Left ventricular and left atrial diastolic pressures are essentially

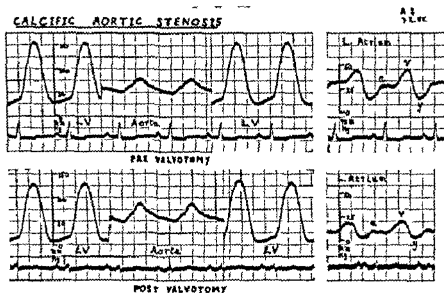


Fig 706—Pressure pulses from aorta left ventricle and left atrium in a case of aortic stenosis with left ventricular failure before and after aortic valvotomy showing a typical steep y descent in the left atrial tracing

the same potential differences being offset by unobstructed flow The appearances are similar to those seen in mitral incompetence (Owen and Wood 1955) In the tracing illustrated which was obtained from a case of aortic stenosis with left ventricular failure and recorded during aortic valvotomy the Ry x ratio (q x) was 5 4 before and 6 after the operation

GALLOP RHYTHM

When the rhythm of the heart sounds has three instead of two beats per cycle one may properly speak of triple rhythm The term covers all

varieties of cadence in which three heart sounds are heard Gallop rhythm, on the other hand should have a stricter meaning and should be applied only to specified forms of triple rhythm as explained subsequently

Mechanism Phonocardiography proves that there are really four normal heart sounds the atrial or presystolic sound associated with atrial systole and late ventricular distension the first heart sound due to mitral and tricuspid valve closure the second heart sound due to closure of the aortic and pulmonary valves and the third heart sound which is attributed to sudden distension of the ventricles in the phase of rapid filling Each of these sounds is thus composed of at least two elements Although these elements may not be strictly synchronous they are sufficiently so as a rule to produce but one obvious sound to the untrained human ear On more careful analysis however they may often be separated sufficiently to be detected individually by auscultation and we may then speak of split sounds The word split describes the sound well and also indicates the mechanism of its production The term reduplication is often used instead, but has less to recommend it for it bears an accidental onomatopœtic resemblance to the sound of presystolic gallop and it is illogical to apply a word that means doubling to an act of division Split sounds do not give the cadence of triple rhythm because of the close proximity of the separated elements

The extra sound that is responsible for triple rhythm is usually an exaggerated atrial sound the third heart sound or a summation of the two Occasionally it is an additional systolic sound of unknown origin

Presystolic (atrial) gallop An audible atrial sound associated with a normal or slightly prolonged P R interval gives rise to triple rhythm with an amphibrachic metre (u — u) As it may be felt as well as heard it is best appreciated by means of a rigid wooden stethoscope or with the naked ear so that tactile and aural senses may be allied The presystolic sound is soft and dull, and is usually localised to the region of the apex beat where it is pathognomonic of left ventricular stress occasionally it is heard best at the left border of the sternum when it may denote right ventricular stress The extra sound occurs about 0 15 second after the onset of the P wave and about 0 07 second after the onset of atrial systole (Weitzman 1955) it is attributed to extra forceful ventricular distension If the P R interval is sufficiently prolonged, the atrial sound may fall in mid or early diastole if the heart rate is fast its true relation to the first or second heart sound cannot be determined clinically unless transient slowing is induced by means of carotid sinus compression Presystolic gallop is never heard when there is atrial fibrillation

Presystolic gallop is a sign of ventricular stress That the atrial reserve is being used means that the handicapped ventricle has asked for (and is receiving) extra presystolic stretch to enable it to meet its commitments The sign does not therefore denote failure but a particular form of compensated state

Left atrial gallop is heard chiefly in essential hypertension and following cardiac infarction, right atrial gallop in severe pulmonary hypertension or stenosis.

Normal third heart sound When the extra sound occurs shortly after the second heart sound giving the metre of a dactyl (— ∪ ∪) it may represent a normal or abnormal third heart sound (fig 7 07) The normal third heart

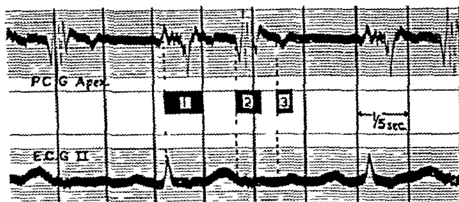


Fig 7 0 —Phonocard ogram show ing a normal th rd heart sound
(R art ; f D F D H (m)

sound was well described by Gibson (1907) It is soft low pitched, and usually accompanied by a palpable shock, it is more or less localised to the apex beat, varies in intensity with respiration and is accentuated when the subject lies on the left side especially if the venous pressure is raised by pressing on the abdomen It may be heard in the great majority of children (but not in infants) in about 50 per cent of young adults occasionally in the middle aged and rarely in the elderly Phonocardiography shows that the third heart sound synchronises with the latter half of the descending limb of the v wave of the jugular phlebogram and therefore with the period of rapid ventricular filling (Ohm 1913) It is attributed to sudden distension of the left ventricle at this time—about 0 15 second after aortic valve closure

Protodiastolic gallop Abnormal third heart sounds are common in mitral incompetence, constrictive pericarditis and in advanced heart failure from any cause especially when there is atrial fibrillation The age and clinical condition of the patient emphasise their significance The term proto diastolic applied to this form of gallop is unfortunate for physiologically protodiastole is the first part of ventricular relaxation immediately before and incorporating the second heart sound the second phase in diastole is isometric relaxation with all valves closed the third is the rapid f phase with atrial pressures chasing ventricular pressures to the 3 and it is towards the end of this third diastolic period that the extra

occurs *diastolic gallop* would describe it more simply and without this inaccuracy and would still be sufficiently descriptive to distinguish it from other forms of gallop

Left ventricular diastolic gallop implies a raised left atrial pressure and rapid left ventricular filling, and therefore denies mitral stenosis it also implies absence of those conditions which accentuate the third heart sound without failure e g organic mitral incompetence and Pick's disease, thus by common use the term has come to mean triple rhythm due to an abnormal third heart sound resulting from left ventricular failure or near failure Whether or not it can be due to some alteration of myocardial tone independent of overloading is still uncertain

Right ventricular diastolic gallop has a similar meaning in relation to right ventricular physiology and at once denies tricuspid stenosis

(4) *Summation gallop* Summation of atrial and third heart sounds can only occur when there is tachycardia or when the P R interval is sufficiently prolonged With tachycardia the metre may seem to be anapaestic (u u —) dactylic (— u u) or amphibrachic (u — u) according to the fancy of the listener for the extra sound occurs in mid diastole Summation sounds have no clinical significance if they disappear when the heart is slowed by carotid sinus compression (summation gallop) on the other hand such slowing may reveal an atrial sound or a normal or abnormal third heart sound

(5) *Extra systolic sounds* It is not uncommon for an extra sound to occur during ventricular systole Excluding vascular ejection clicks (q v) there are three varieties—the systolic click of left sided pneumothorax lesser systolic clicks possibly associated with pleuro pericardial adhesions and a third type in which the extra sound is dull and muffled and in no way like a click Patients with partial left sided pneumothorax may complain of a loud clicking or bubbling noise synchronous with the heart beat It may be so loud that it can be heard at a distance of several feet from the patient it varies markedly with respiration and with change of posture and is always transient It is occasioned by the activities of bubbles of air between the heart and surrounding structures and only occurs when the pneumothorax is small, so that clinically it is a late development, appearing when most of the air has been absorbed (Scadding and Wood 1939) Lesser systolic clicks are heard from time to time in subjects who are perfectly well and according to Gallavardin (1913) may depend upon pleuro pericardial adhesions In these cases the extra sound resembles a click but is not so impressive nor so variable as that associated with left sided pneumothorax It may last for weeks months or years and may come and go without apparent reason The third type (systolic gallop) is distinguished from greater and lesser systolic click by the character of the extra sound which is dull and muffled Its mechanism is not yet understood It is uncommon and when heard may be disregarded for it occurs in apparently healthy persons

Note on nomenclature Introduced by Professor Bouillaud analysed and popularized by Potain (1876) the term gallop rhythm originally referred to that variety of triple rhythm which denoted impending or actual left ventricular failure and in the presence of tachycardia is marvellously adapted to the sound it designates But by 1900 Potain had extended the meaning of the bruit de galop to include presystolic protodiastolic and systolic varieties attributing these different metres to the same factors that are to day held responsible Thus historically it is not incorrect to regard gallop rhythm and triple rhythm as synonyms but there is an advantage in excluding certain types of triple rhythm from the cadences embraced by the bruit de galop Thus it is preferable and customary to speak of presystolic (atrial) diastolic systolic and summation gallops on the one hand and of systolic clicks the third heart sound and the opening snap of mitral stenosis on the other

PULSUS ALTERNANS



Pulsus alternans (Traube 1872) is characterised by a regular rhythm in which the pulse beats are stronger and weaker alternately It may be detected by palpation or more easily by sphygmomanometry there being a difference of 5 to 20 mm of mercury in the systolic pressure between alternate beats It may be found in association with left ventricular failure toxic carditis, paroxysmal tachycardia or auricular flutter Clinically alternation may be maintained as long as the heart is labouring occasionally for as long as two or three years Latent alternation may become manifest when the heart beats faster Experimentally under favourable conditions e g when the heart is poisoned by certain drugs including digitalis when it is made to beat very fast or when its blood supply is curtailed short periods of alternation may follow a premature ectopic beat (Mackenzie 1907–8) or a dropped beat (Hering 1908) Sphygmograms show that pulsus alternans may begin abruptly either with an unusually large beat or with a small beat (Lewis 1925) and that the sum of a large and small beat equals the sum of two normal beats (Gaskell 1882) Pulsus alternans is exaggerated by any agent or manœuvre that lowers the venous filling pressure, and diminished by any procedure that raises the venous filling pressure (Friedman *et al* 1953)

No thoroughly satisfactory hypothesis has been evolved to explain pulsus alternans It is generally believed that fewer muscle fibres contract with the weaker beats than with the stronger owing to the development of a state of partial refractoriness (Lewis 1925) fibres which do not contract with one beat recover in time for the next other fibres which contract with the first beat are still refractory and therefore unready for the second In other words there is a state of 2 1 partial ventricular response But if this were true all the beats should be weaker than normal the hypothesis does not explain the stronger beats Another suggestion is that pulsus alternans depends upon a disorder of ventricular relaxation for the ventricles hold

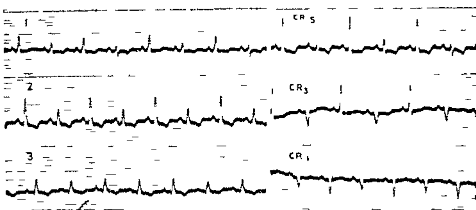


Fig 7 08—Electrical alternation in a case of malignant disease involving the pericardium pulsus alternans was present

more blood with the stronger beats and less with the weaker (Straub 1917)

Pulsus alternans should not be confused with electrical alternation (fig 7 08) nor with coupled beats due to premature systoles Electrical alternation is sometimes associated with pulsus alternans however as in the case illustrated

CHEYNE STOKES BREATHING

Periodic breathing was described by Cheyne (1818) in what was probably a case of hypertensive heart failure with right hemiplegia For several days his breathing was irregular it would entirely cease for a quarter of a minute then it would become perceptible though very low then by degrees it became heaving and quick and then it would gradually cease again this revolution in the state of his breathing occupied about a minute Stokes (1854) connected the phenomenon with serious heart disease

Mechanism In spontaneous Cheyne Stokes breathing, the respiratory centre is depressed and appears to be insensitive to a normal carbon dioxide tension but still responds to a raised pCO_2 and reflexly to sufficient anoxia With normal arterial oxygen and CO_2 tensions breathing therefore stops, during the apnœic phase the arterial pO_2 falls and the arterial pCO_2 rises and sooner or later this powerful combination excites the sluggish respiratory centre during the dyspnœic phase however the abnormal blood gas tensions are soon corrected and breathing again stops The crescendo character of the dyspnœic phase may be due to time lag when respiration starts and carbon dioxide in the blood entering the lungs is blown off blood which has already passed the pulmonary capillaries must have a higher carbon dioxide tension and lower oxygen tension than that which galvanised the respiratory centre into action this takes 5 to 10 seconds to reach the respiratory centre in normal subjects and an average of about 20 to 25 seconds in patients with left ventricular failure

The administration of carbon dioxide abolishes Cheyne-Stokes breathing by maintaining an arterial pCO_2 high enough to excite the respiratory centre. The inhalation of oxygen prolongs the period of apnœa because it then takes longer for an effective anoxic stimulus to develop. Voluntary hyperventilation precipitates periodic breathing by ensuring an initial period during which the blood gas tensions are such that the respiratory centre must lie idle. Natural sleep, barbiturates and morphine aggravate Cheyne Stokes breathing by further depressing the respiratory centre.

Clinical features Periodic breathing may result from a cerebral lesion, e g a head injury or a cerebral vascular accident, or from left ventricular failure, usually in patients with hypertensive or ischæmic heart disease when sclerosis of cerebral vessels may be associated.

The cerebral type is characterised by a rise of blood pressure and pulse rate during the dyspnœic phase (Eyster 1906); in patients with left ventricular failure the central venous pressure and blood pressure rise during dyspnœa, the pulse rate and fore arm blood flow during apnœa (Sharpey Schafer 1948). Rhythmic variation in the size of the pupils may also be observed: they dilate during dyspnœa and contract during apnœa.

Cheyne Stokes breathing may cause insomnia by waking the patient at the height of the dyspnœic phase.

RIGHT VENTRICULAR FAILURE, CONGESTIVE HEART FAILURE

When the right ventricle fails to discharge its contents adequately, the pressure in the right atrium and venæ cavæ rises, the liver becomes enlarged and tender, and dependent œdema usually develops.

ETIOLOGY

Right ventricular failure in its purest form results from pulmonary hypertension, massive pulmonary embolism, pulmonary stenosis or atrial septal defect.

The term congestive heart failure is preferable when systemic congestion complicates mitral stenosis, left ventricular failure, rheumatic or other forms of carditis, thyrotoxicosis or other hyperkinetic circulatory states, serious abnormalities of rhythm, ventricular septal defect, or other diseases affecting the heart as a whole.

CLINICAL FEATURES

Elevation of the venous pressure. By far the most important sign of right ventricular failure is a rise of systemic venous blood pressure. Its detection depends essentially upon clinical observation, especially upon inspection of the internal jugular pulse (q v).

In untreated heart failure the venous pressure averages about 10 cm above the sternal angle at 45 degrees, but the range is considerable (3 to 25 cm). The chief venous pulse wave may be a or v or the return of

y to the z point When there is auricular fibrillation and no x descent it is difficult to distinguish the venous pulse of heart failure from tricuspid incompetence, but on the whole v is bigger in tricuspid incompetence and is transmitted more obviously to the liver Clinically the distinction rarely matters much for tricuspid incompetence is nearly always functional and secondary to right ventricular dilatation and failure

When the venous pressure is within normal limits at rest, it may yet rise unduly on slight exertion and may take several minutes to regain its resting level This is a manifestation of limited cardiac reserve The jugular venous pressure normally falls on exertion because increased ventilation lowers the mean intrathoracic pressure the true filling pressure tends to rise

The cause of the elevated venous pressure in congestive heart failure has already been discussed (page 267)

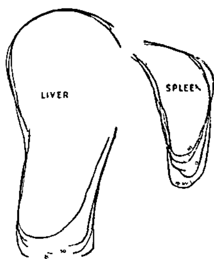


Fig 7 09—Tracings of serial skiagrams of liver and spleen opacified by means of thorotrast demonstrating the rapid shrinkage of the liver and spleen which occurs when 1 5 mg of digoxin is administered to a case of congestive failure

Enlargement and tenderness of the liver Hepatic distension may cause spontaneous pain in the right hypochondrium especially when it develops quickly as in failure from paroxysmal tachycardia Sometimes the pain is related to effort

Palpation of the liver should be preceded by inspection and percussion Epigastric fullness and dullness to percussion are characteristic of hepatic engorgement on the other hand epigastric flattening or concavity with resonance to percussion is incompatible with it Percussion of the right hypochondrium during the different phases of respiration often reveals the size of the liver with as much precision as palpation The latter is best carried out with the left hand the physician standing to the patient s left It may be helpful to place the right hand high up under the right lower ribs and to exert forward pressure in order to push the liver towards the anterior abdominal wall if the organ is distended its edge can be felt with the forefinger of the left hand as it moves downwards during inspiration Pressure over an engorged liver is painful Hepatic pulsation may be felt in cases of tricuspid incompetence expansion coinciding with ventricular systole If there is ascites an enlarged liver may be recognised by dipping , a repeated sudden pressure of the hand over the region of the liver when a sensation like that of a patella tap or like that of ballotting a fœtus in utero may be appreciated The liver

shrinks as engorgement is relieved (fig 7 09) and this may be demonstrated within half an hour of giving 1 5 mg of digoxin intravenously (Wood 1940)

Anatomically the liver almost invariably shows centrilobular hepatic *necrosis in cases of congestive heart failure*—Hepatic function is disturbed to the extent of a raised serum bilirubin (usually short of frank jaundice) increased urobilinogen in the urine and diminished excretion of brom sulphalein alkaline phosphatase total and differential serum proteins and the serum colloidal gold precipitation test are all usually normal (Sherlock 1951)

After repeated attacks of failure or after years of persistent distension cirrhotic changes may occur but they are usually unimportant and rarely interfere seriously with hepatic function or with portal drainage The most important clinical sign of seriously impaired hepatic function appears to be the bright palmar flush often associated with warm hands and digital throbbing despite obviously advanced heart failure and evidence of a low cardiac output



Fig 7 10—Dependent œdema in congestive heart failure

Œdema Of the three classic signs of congestive heart failure œdema is the least reliable It may be absent when the venous pressure is high and gross when it is not so high It is frequently absent in acute cases especially in children Cardiac œdema is essentially dependent (fig 7 10) but is occasionally observed in the face and is not infrequent in the arms It is of course accompanied or preceded by oliguria and by a gain in body weight in fact as much as six litres of fluid may collect in the tissue spaces before pitting œdema is necessarily demonstrable

The mechanism of the two most important forms of œdema cardiac and nephritic is not yet fully understood In both as a rule the protein content of fluid samples is low (less than 1 G per cent) the venous pressure is raised, and the blood volume is increased (Warren and Stead 1944) but there are exceptions Thus in chronic anæmia with congestive heart failure the blood volume is much diminished (Sharpey Schafer 1944) Increased capillary permeability is excluded by the low protein content of the œdema fluid moreover the theory that anoxia might be the cause of such capillary

dysfunction is unlikely in that cardiac œdema may be associated with a high cardiac output and normal arterial oxygen saturation as in arterio venous aneurysm Elevation of the hydrostatic pressure at the venous end of the capillaries must play a part but not necessarily a major part In partial superior vena cava obstruction for example œdema does not occur until the venous pressure is very much higher than it is in heart failure and ligation of the inferior vena cava below the renal veins in cases of heart failure relieves œdema in the legs (Cossio and Perratta 1949) Reduction of renal blood flow to about 25 per cent of normal in most cases of con gestive failure has been demonstrated (Merrill 1946) and there is a considerable degree of sodium retention according to Merrill and Cargill (1948) œdema occurs when the filtration rate falls below 70 to 80 ml /litre tubular reabsorption being almost complete Merrill and Cargill (1947) demonstrated similar impairment of renal blood flow and filtration rate in a case of thyrotoxic heart failure with high cardiac output

There is also evidence that patients with congestive heart failure excrete an anti diuretic substance in the urine and that this is not pitressin (Bercu Rokaw and Massie 1950) This opens up yet another line of approach to this fascinating problem

OTHER MANIFESTATIONS OF CONGESTIVE HEART FAILURE

General symptoms Owing to the absence of pulmonary venous congestion breathlessness is far less pronounced than in left heart failure and there is no orthopnœa The low cardiac output is reflected by fatigue or by a sense of heaviness in the limbs and on effort there may be dizziness or blurring of vision In severe cases vomiting may be troublesome and it is sometimes difficult to know whether heart failure or digitalis therapy is responsible

Urinary findings Oliguria, of course is associated with œdema The urine which is rich in colour and of high specific gravity often contains albumin, leucocytes, red cells, and both hyaline and granular casts

Hydrothorax may occur from left or right ventricular failure and though usually bilateral tends to be left sided with the former and right sided with the latter (Bedford and Lovibond 1941) It should be remembered that the visceral pleura is drained by a venous plexus which is composed of both bronchial and pulmonary venous radicles In typical instances the fluid is a transudate with a specific gravity ranging between 1 015 and 1 020 protein is often between two and three per cent and there may be moderate numbers of leucocytes and red cells Unsuspected pulmonary infarction may further complicate the picture increasing the specific gravity the pro tein content the leucocyte count and especially the number of red cells the overlying pleurisy giving rise to an exudate If the fluid is frankly hæmorrhagic associated pulmonary infarction may be diagnosed with confidence

Ascites is less common than hydrothorax and usually implies long standing failure. It is a special feature of tricuspid lesions and of chronic constrictive pericarditis

Hydropericardium is usually of little significance cardiac compression does not occur the electrocardiogram is uninfluenced and there are no symptoms *It is only important in that it alters the size and shape of the* heart shadow and so may confuse radiographic observations

Cerebral symptoms Difficulty in concentration impairment of memory mental confusion change of character and manic depressive paranoid or other psychotic states are by no means rare accompaniments of heart failure They may be due to hypoxia or occasionally to hepatic failure and are encountered particularly in hypertensive of ischæmic heart failure *when cerebral arteriosclerosis may be partly responsible and in severe* anoxic pulmonary heart disease especially when complicated by broncho pneumonia

Cardiac cachexia Patients with chronic heart failure usually lose flesh although loss of weight may be prevented by fluid retention thus wasting may only be noticed after diuresis sometimes it is so great as to warrant the term cachexia Elevation of the basal metabolic rate anorexia impairment *of intestinal function and enforced muscular inactivity may be partly* responsible

Venous thromboses are common in congestive heart failure especially when the cardiac output is low They are responsible for the frequency of pulmonary infarction

Jaundice may develop in severe cases and may be mainly obstructive (McMichael and Sherlock 1945) or mainly hæmolytic, the former depending perhaps upon the raised intra hepatic pressure the latter upon the

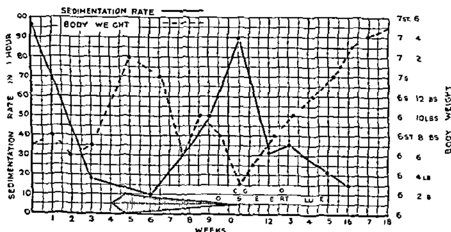


Fig ~ 11—Fall in erythrocyte sedimentation rate resulting from the development of cong st ve f ilure in a case of activ rheumatic carditis

(a) April 14, 1936

(b) May 9, 1936 (after treatment)

destruction of red cells in hæmorrhagic pulmonary infarcts The serum bilirubin is often in the region of 2 mg per cent Itching may occur

Immature red cells are common and may be due to stimulation of the bone marrow by anoxia Polycythæmia may be masked by hydræmia

The erythrocyte sedimentation rate is often retarded by congestive failure (Wood 1936) Figures of 50 to 100 in one hour obtained by the Westergren method in cases of rheumatic carditis myocardial infarction and syphilitic aortic incompetence may drop below 10 with the onset of failure and rise to their former level with recovery (fig 7 11)

The basal metabolic rate is usually raised by about 20 per cent in heart failure as first pointed out by Peabody *et al* (1916) A 10 per cent increase could be due to a great increase of heart weight, for a 300 Gm heart consumes about 20 to 25 ml of oxygen per minute and a failing 600 Gm heart about 50 ml of oxygen per minute (Bing *et al* 1949) The discrepancy has been attributed to extra work performed by the muscles of respiration (Resnik and Friedman 1935)

Radiographic appearances The transverse diameter of the heart is increased by 1 to 2 cm during failure (figs 7 12a and b) In making such measurements care must be taken to exclude apparent enlargement due to raising of the diaphragm by an enlarged liver so that the heart takes up a more horizontal position The superior vena cava throws a denser shadow than usual and the right atrium is more prominent The lesser fissure on the right side may be clearly marked owing to pleural congestion or hydrothorax may be evident

Behaviour of the blood pressure The blood pressure might be expected to fall in congestive heart failure but in fact it may rise fall or remain stationary in the majority of cases it rises There are only two conditions in which heart failure is characteristically associated with a sharp drop of blood pressure acute myocardial infarction and massive pulmonary embolism Conspicuous lowering of the blood pressure associated with heart failure in other diseases is commonly a terminal event The vasoconstriction that maintains the blood pressure when the cardiac output falls is partly reflex and perhaps partly renal in origin It may be recognised clinically by cold extremities and peripheral cyanosis An increased concentration of renin has been found in blood samples obtained from the renal vein in cases of congestive heart failure (Merrill Morrison and Brannon 1946) A powerful pressor agent must be at work to raise the blood pressure in the face of a cardiac output that may be only half the normal resting level In advanced heart failure impairment of hepatic function may lower the blood pressure (Raaschou 1954)

Character of the heart sounds Current terminology still includes such expressions as weak faint or distant heart sounds and tic tac or fœtal rhythms which have been supposed to signify failure or threatened failure Apart from cases of coronary thrombosis, pulmonary embolism and pericardial effusion, weak, faint, or distant heart sounds are commonly due to

obesity, emphysema or well developed thoracic muscles It is doubtful whether tic tac or fœtal rhythm is in any way associated with central heart failure on the other hand it is heard in patients suffering from shock and may be associated with diminution of the blood volume A weak first heart sound associated with a normal second sound is usually due to a P R interval around 0 21 to 0 22 second the mitral cusps then having time to float into apposition before the ventricles contract (Levine 1948)

PHYSIOLOGICAL TESTS FOR CONGESTIVE HEART FAILURE

Although as a rule there are good clinical grounds for being confident whether heart failure is present or not difficulties arise occasionally the following tests may then be enlisted

Valsalva manœuvre

The diastolic hypertension and secondary bradycardia that follow strain in normal individuals are attributed to reflex vasoconstriction from stimulation of carotid and aortic baroreceptors by the diminished stroke output and pulse pressure that follow reduction of the effective filling pressure (fig 5 06) In heart failure however the overloaded ventricle maintains a normal or even increased stroke volume and pulse pressure when its filling pressure is reduced so that the baroreceptors are either not stimulated at all or respond to the increased pulse pressure by causing vasodilatation and a corresponding fall in diastolic pressure (Sharpey Schafer 1955) The square wave in figure 7 13 is due simply to the rise in all

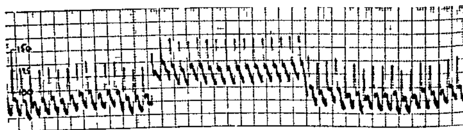


Fig 7 13—Arterial pressure pulse during Valsalva s manœuvre in a case of congestive heart failure showing a square wave effect (see text)

pressures (venous intracardiac pulmonary systemic and of course intrathoracic) that occurs during the period of strain there is no decrease of pulse pressure no diastolic hypertension no overshoot and no secondary bradycardia It is easy enough to note the effect of strain on the pulse pressure and pulse rate at the bedside so the test should have considerable clinical value

Forearm blood flow

A second indirect method of determining whether or not the cardiac output rises in response to an increased or decreased venous filling

pressure is to measure the forearm blood flow when the body is horizontal and when it is tilted legs down at an angle of 45 degrees or [illegible] In normal subjects the cardiac output rises in the horizontal position and falls in the tilted (legs down) position in response to well known postural changes in venous filling pressure and there are corresponding changes in forearm blood flow which receives its share of the output In other words when the subject lies flat the forearm flow rises and when he is tilted legs down it falls In patients with heart failure however the forearm blood flow responds paradoxically to changes of posture in view of the changed relationship of venous pressure to output when either ventricle is over loaded (Brigden and Sharpey Schafer 1950) This test might have clinical value if the changes in forearm flow could be detected by means of a skin temperature thermometer or photoelectric cell (recording digital pulsation)

Direct measurement of intracardiac pressures and cardiac output

Cardiac catheterisation makes it possible to measure both atrial pressures right ventricular diastolic pressure and cardiac output more or less at the same time In congestive heart failure all these pressures are raised (fig 7 14) the arterio venous oxygen difference is over 50 ml per litre

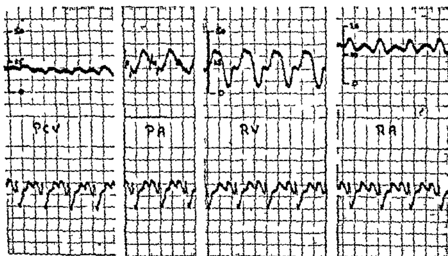


Fig 7 14 – Elevated pressures in both atria in a case of congestive heart failure involving both ventricles

the cardiac output less than 4 5 litres per minute at rest and the cardiac index (C O per square metre of body surface) below 3 In pure right ventricular failure the findings are similar except that the left atrial pressure is normal If the patient is tilted about 45 degrees legs down or if venous tourniquets are applied to the thighs the right atrial pressure falls and the cardiac output rises in accordance with Starling s law On effort

the A V difference increases greatly the output little if at all despite a considerable *rise of right atrial pressure and tachycardia*

PROGNOSIS OF HEART FAILURE

When left ventricular failure develops in the natural course of hypertensive or aortic valve disease the prognosis in untreated cases is poor patients seldom living more than eighteen months after the onset of orthopnœa or paroxysmal cardiac dyspnœa but few die before clinical signs of chronic systemic congestion become apparent Modern treatment *however* has greatly improved the prognosis of left ventricular failure particularly in hypertensive heart disease and aortic stenosis and life may be prolonged for years

The natural prognosis may be less unfavourable when acute myocardial infarction is responsible because if the patient survives the acute phase he may make a good recovery and although the average life expectancy is *still only* about 5 years the chances of much *longer survival are not* remote

The outlook is entirely different when left ventricular failure complicates acute nephritis here complete recovery may be anticipated The ultimate prognosis depends upon the subsequent course of the nephritis Similar remarks apply to other forms of hypertension which are transient or which can be treated successfully

The prognosis of right ventricular failure or congestive heart failure depends very much upon its cause When associated with diseases that can be cured or improved such as mitral stenosis or thyrotoxicosis the outlook is excellent On the other hand when it occurs in the natural course of chronic and incurable heart disease few patients survive more than a year or two Between these extremes are cases of incurable heart disease in which failure is precipitated by some adverse factor which is either transient or which can be improved or cured Undue physical work pregnancy infection disturbances of rhythm and pulmonary embolism provide examples of such factors

TREATMENT

Since the measures used in the treatment of left *and right ventricular* failure are practically the same they will be considered together

Rest in bed or in a comfortable armchair is essential and should be continued for a minimum period of three weeks If signs of failure do not disappear within a few days of instituting adequate therapy the period of rest should be extended to six weeks The patient should be nursed against a back rest at an angle of about 60 degrees whether orthopnœic or not for there is no easier way of lowering the right atrial pressure and so unloading the overburdened heart if the legs are lowered so much the better —hence the value of an armchair or cardiac bed *Meals* should be small in quantity and fluids limited to about two pints daily If the *sodium intake*

Fig 7 15—Typical effect of digitalis on the venous pressure or right atrial pressure in four cases of congestive heart failure

Fig 7 16—Typical effect of dig talis on the blood pr ssure pulse rate right atr l pressure and cardiac output in a case of hyp rt ns e heart failure ith normal rhythm

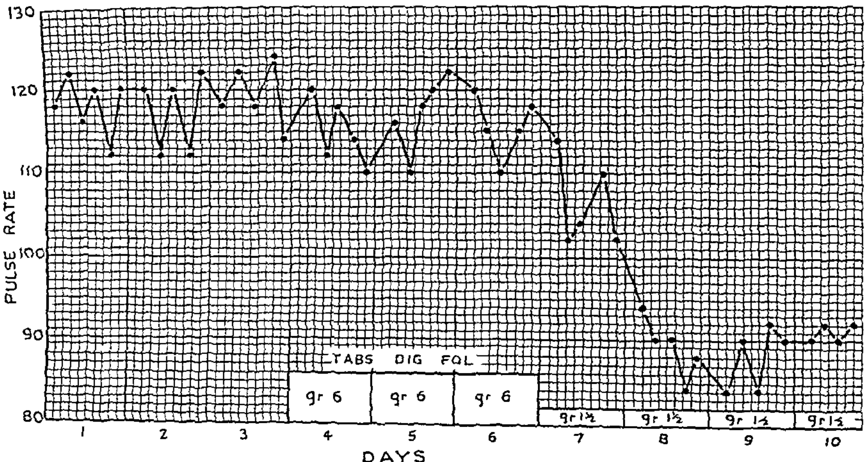


Fig ~17—Graph how ng the p onounc d lo ng ff t of dig talis in a c of congestive failure w th normal rhythm due to active rheumatic carditis

can be limited to 0 5 G daily however there is no need to restrict fluids Correct treatment of heart failure usually serves as the best hypnotic but if insomnia is troublesome at first there should be no hesitation in using powerful sedatives

Venesection deserves a better reputation It has fallen out of favour because similar results may be obtained by means of certain drugs, but it offers a quick and sure way of lowering the venous pressure and should not be abandoned About 600 to 750 ml of blood may be withdrawn

Digitalis obtained from the common foxglove and discovered to be a cure for cardiac dropsy by William Withering in 1785 is beneficial whether there is auricular fibrillation or normal rhythm and whether the pulse rate is fast or slow It lowers the venous pressure (fig 7 15) raises the blood pressure (fig 7 16) slows the heart rate (fig 7 17) relieves hepatic distension (fig 7 09) increases the vital capacity shortens the pulmonary circulation time (fig 7 18) increases the cardiac output (fig 7 16) and encourages diuresis (fig 7 19) Its good effects cannot be attributed to a direct venous pressure lowering action as suggested by McMichael and Sharpey Schafer (1944) for digitalis does not lower a raised venous pressure in the absence of heart failure (fig 7 20 from Wood and Paulett 1949) and in cases of left ventricular failure it raises the output reduces

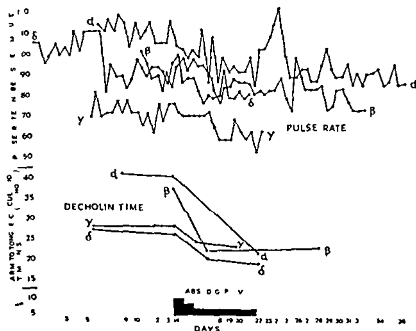


Fig 7 18—The action of digitalis on the arm to-tongue circulation time and on the pulse rate in four cases of left ventricular failure with normal rhythm

passive pulmonary hypertension and therefore lowers left atrial pressure without altering the normal right ventricular diastolic pressure (Harvey *et al* 1949) The original belief that digitalis improves the function of the heart by virtue of its direct action on the myocardium is probably correct In normal controls increase of myocardial tone may make the heart smaller and may reduce its output (Stewart *et al* 1938)

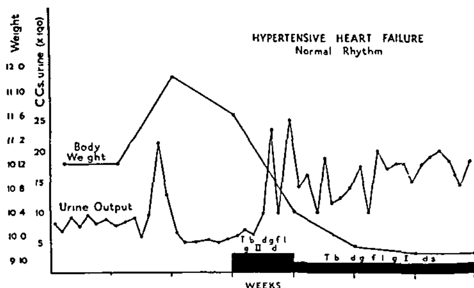


Fig 7 19—Chart showing considerable diuresis resulting from the administration of digitalis to a case of hypertensive heart failure with normal rhythm

Digitalis should not be withheld when heart failure is due to cardiac ischæmia, cor pulmonale or heart block

In ischæmic heart disease digitalis was believed to be dangerous because it was shown to encourage ventricular tachycardia or fibrillation in cats subjected to experimental cardiac infarction (e g Travell Gold and Modell 1938) and because the microscopic myocardial lesions caused by digitalis in cats (Buchner 1934) closely resembling those produced by acetylcholine and prolonged vagal stimulation (Hall *et al* 1937) were likewise attributed to coronary vasoconstriction because they could be prevented by means of coronary vasodilators such as aminophylline (Kyser Ginsberg and Gilbert 1946) and because digitalis is known to have a cholinergic action (Danielopolu 1946) But in clinical practice digitalis in therapeutic doses has no effect whatever on the severity duration or frequency of attacks of angina pectoris (Gold *et al* 1938) and both digitalis and ouabain have proved efficient treatment for cardiogenic shock following acute cardiac infarction (Gorlin and Robin 1955) as well as for ordinary ischæmic heart failure Finally Bing *et al* (1950) have proved that strophanthus has no effect on coronary blood flow

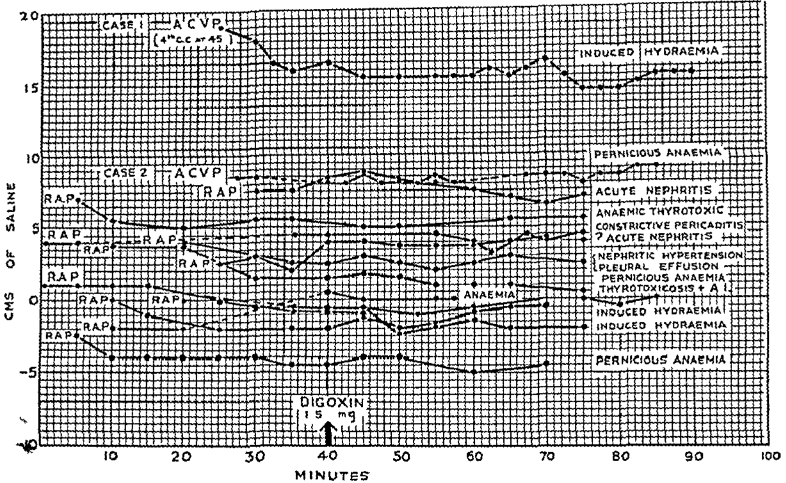


Fig. 7 20—Chart illustrating the failure of digitalis to lower the right atrial pressure in twelve cases in which it was raised from causes other than congestive failure

Digitalis tended to be withheld in cases of cor pulmonale when a raised venous pressure was associated with signs of a raised cardiac output because Howarth McMichael and Sharpey Schafer (1947) had shown that the high output (which was compensatory and beneficial) fell if the venous pressure was lowered (by venesection for example) and at that time these workers believed that digitalis was a primary venous pressure lowering agent moreover digitalis seemed to be of little value clinically unless the cardiac output was obviously low The hypothesis that digitalis is a primary venous pressure lowering agent has since been abandoned (McMichael 1952) and it is now generally believed that digitalis is beneficial in cor pulmonale if there is true heart failure but not otherwise it may certainly be tried, however, without fear of harming the patient

It is doubtful if there are any real contra indications to digitalis in therapeutic doses The suggestion that it encouraged thrombosis has been refuted (Cathcart and Blood 1950) Potassium-depletion appears to make the heart hypersensitive to digitalis (Friedman and Bine 1948 Lown *et al* 1951) Peptic ulcers and other disorders of the gut that react unfavourably to cholinergic agents may be aggravated by digitalis

For routine purposes the dose of digitalis should be 3 grains (0 2 G) of the powdered leaf t d s on the first day 2 grains (0 13 G) t d s on the second and 1 grain (65 mg) t d s thereafter until demonstrable improvement or evidence of intoxication occurs when it may be reduced to 1 grain (65 mg) b i d Heavy loading doses should only be given when it is known that the patient has received no digitalis for at least one month Other methods of administering digitalis are described on page 255

Strophanthin may be preferred when a quick action is desired especially if a cumulative effect is not wanted A single dose of Ouabain 1 0 mg intravenously may raise the cardiac output in cases of heart failure without affecting the venous pressure (McMichael 1948) and so presumably acts directly on the heart Like intravenous digoxin it also has a conspicuous pressor effect and slows the pulse rate Strophanthin may be the drug of choice in collapsed cases of cor pulmonale

Mercurial diuretics were discovered more or less by accident at the Wenckebach clinic in Vienna in 1919 when it was noticed that a new anti syphilitic mercurial substance novasurol when injected into a dehydrated young girl with congenital syphilis provoked unexpected diuresis (Vogl 1950) Novasurol however was painful and toxic and was soon replaced by the more potent yet more benign salyrgan (Bernheim 1924) Theophylline was combined with the organic mercurial component in 1928 (von Issekutz and von Vegh) in the hope that a summation effect would increase the diuresis but the combination introduced as novurit proved less painful and more effective than expected being better absorbed and more efficiently excreted owing to a fundamental change in the structure of the substance when theophylline was incorporated (de Graff Batterman and Lehman 1938) This is the basis of mersalyl (B P) modern salyrgan

(Bayer) neptal (M & B) esidrone (Ciba) and the American mercurophylline and mercuhydrin All these substances contain about 40 per cent of metallic mercury ampoules for injection contain 10 per cent of the drug and 5 per cent of theophylline The usual dose is 2 ml intramuscularly which contains 80 mg of metallic mercury and 0 1 Gm of theophylline It may be repeated every third or fourth day preferably with ammonium chloride gr. 30 t d s on the day of the injection to replace chloride loss

In mercaptomerin (thiomerin) the organic mercurial substance is combined with a mercaptide group instead of theophylline this has greatly decreased toxicity while preserving full diuretic potency moreover thiomerin may be given subcutaneously for it causes very little local irritation and is therefore practically painless (Batterman *et al* 1949)

From time to time attempts have been made to encourage oral mercurial diuretics but in the past they have never withstood prolonged clinical trials being too irritating to the gastric mucosa and too inefficient The latest is merchloran (chlormerodrin) in a dose of 2 tablets each equivalent to 10 mg of mercury three or four times a day (Moyer *et al* 1952) With these doses however gastro intestinal symptoms are frequent and as a rule only 1 tablet is given three or four times daily at the start and once or twice daily for maintenance

Mersalyl rectal suppositories which contain 0 4 Gm of mersalyl and 0 2 Gm of theophylline usually provoke severe local burning pain and cannot be recommended

Mercurial diuretics act by discouraging tubular reabsorption of sodium potassium and chloride (Blumgart *et al* , 1934), and so remove œdema in water logged patients and cause dehydration in those without œdema (De Vries 1946) The blood volume declines and the venous pressure falls secondarily If the heart is overloaded the cardiac output rises and the whole functional state of the circulation improves These effects are gradual beginning an hour or two after the injection and depend upon the degree of diuresis (Vohni and Levitt 1939) A much earlier and more rapid fall of venous pressure may result from the incorporated theophylline (Pugh and Wyndham 1949) If the right ventricle is not overloaded its output probably falls and this helps to decongest the lungs in cases of left ventricular failure or mitral stenosis (Friedman *et al* 1935) Thus mersalyl has proved an excellent drug for preventing paroxysmal cardiac dyspnœa (fig 7 21)

Toxic reactions are rare but high fever and rigors have been encountered (Foster and Naylor 1951)

Sudden death has been reported after intravenous injections This is a direct toxic effect of a relatively high concentration of mercury on the heart death occurring from ventricular fibrillation or asystole within 1 to 3 minutes of the injection. It may occur after the first injection, when previous injections seem to have been well tolerated or after warnings of disaster have been noted on previous occasions (Kaufman 1948) Sudden

death of this kind is very rare after intramuscular or subcutaneous injections Ventricular fibrillation or asystole however may also occur after a massive diuresis it has been suggested that the combination of potassium depletion (which sensitises the heart to digitalis) and digitalis concentration may be responsible

Considerable weakness and fatigue may follow the use of mercurial diuretics and have been attributed to sodium potassium and chloride depletion the feeling of exhaustion occurs especially the day after the

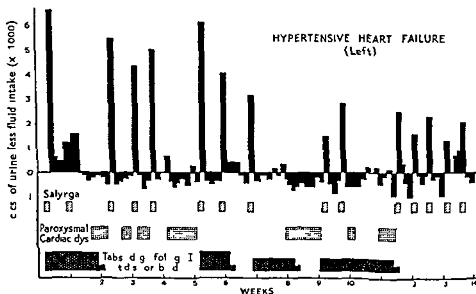


Fig 7 21—Chart illustrating the beneficial effect of mercurial diuretics in preventing paroxysmal cardiac dypsnœa Digitalis was less effective

injection and is only partly relieved by potassium and chloride Nausea and vomiting colic or diarrhœa may be due to digitalis concentration An attack of gout may be precipitated by the dehydration in susceptible individuals Patients with prostatic symptoms may develop acute retention as a result of distension of the bladder and should be warned to void urine hourly after an injection without waiting for the desire Abdominal cramps are due to sodium depletion Hiccough and drowsiness suggest uræmia and usually mean that treatment has been too intense and that the blood sodium and chloride are too low This is rare unless the patient is also on a low sodium diet

Toxic nephrosis, characterised by tubular degeneration and calcification is encountered occasionally usually after prolonged administration (Waife and Pratt 1946)

The drug should not be stopped owing to a poor initial response for the result of the second or third dose coinciding perhaps with the beneficial

effect of rest and digitalis may exceed expectations The only contra indications are known hypersensitivity and acute nephritis

Other diuretics *Mictine* in doses of 200 to 600 mg t d s for two consecutive days each week is the most powerful oral diuretic now available and is usually well tolerated Of the xanthines *theobromine* 0 5 G is the most potent it is best given in the form of 1 0 G of diuretin (theobromine and sodium salicylate) which is more soluble

A low sodium diet has proved a most effective way of relieving obstinate œdema (Schroeder 1941) and preventing paroxysmal cardiac dyspnœa The object is to reduce the sodium intake to the order of 0 5 G daily so that it is impossible for the tissues to hold much fluid The blood volume is thus reduced and the venous pressure lowered The function of the overloaded heart improves as it does after venesection Both the milk diet of Karell (1866) and the rice diet of Kempner (1944 1946) owe their diuretic effects to their low sodium content

The following diet has been constructed from tables giving the com position of numerous foods compiled by McCance and Widdowson (1946) The first figure after each substance gives the amount of sodium in mgs per 100 G of foodstuff The second figure gives the approximate calorific value of the food per mg of sodium content Obviously the best foods are those with a low first figure and a high second figure For the first 48 hours it is a good plan to give nothing but fruit in any form, fruit juice drinks sugar rice and diluted milk Mercurial diuretics should not as a rule be given more than two or three times with this diet the combination causing too much sodium and chloride depletion uræmia which may prove fatal may then develop (Shroeder 1949 Black and Litchfield 1951)

LOW SODIUM DIET

CEREALS

Per i tted			*Doubtful*			*Fo bidden*		
Arrowroot	4 8	72	Currant bread	164	2	Bread	393	0 7
Barley	0 8	150	Sweet biscuits	216	3	B cuits	400	0 8
Cornflour	52	7	Rusks	200	2	Cornflakes	1 050	0 3
Flour	2 5	170				Grapenuts	658	0 5
Macaroni	7 9	15				Post Toasties	810	0 5
Oatmeal	33	11				Ryvita	615	0 5
R c	2	60				Vita weat	615	0 5
Sago	3 4	100						
Semolina	12	30						
Shredd d Wheat	16	22						
Tapioca	4	86						

NOTE

Biscuits Water biscuits and cream crackers contain the most sodium Oatmeal biscuits made without salt and with lard instead of margarine are recommended

Breakfast cereals Oatmeal porridge should be made without salt and with

equal parts of milk and water Shredded wheat with diluted milk and plenty of sugar is recommended

Milk puddings Milk should be diluted with equal parts of water margarine must not be used

Flour sauces Make without salt and with equal parts of milk and vegetable water Use dripping instead of margarine

Bread Home made bread made with yeast flour lard and milk without salt is allowed

DAIRY PRODUCE AND FATS

Permitted			*Doubtful*			*Forbidden*		
Butter (fresh)	223	3 5	Milk (fresh)	50	1 2	Cheese	600	0 5
Cream cheese (home made)	110	8	Milk (sweet condensed)	143	2	Egg white	192	0 2
Cream	31	13				Margarine	318	0 5
Egg yolk	50	7				Butter (salted)		
Olive oil	0 1	9 -90						
Lard	2	450						
Dripping	5	00						
Suet	25	44						

NOTE

Butter may be kneaded in water to reduce its salt content

Home made cream cheese must be made without salt

Dilute milk with half its volume of water

Use olive oil dripping lard or suet in cooking instead of butter or margarine whenever possible

MEAT POULTRY AND GAME

Permitted			*Doubtful*			*Forbidden*		
Roast beef	6	6	Chicken	80	2	Bacon	1 200	0 3
Grilled steak	67	5	Duck	195	1 5	Beef (silverside)	1 470	0 2
Stewed steak	38	5 5	Goose	145	2	Brains	150	0 7
Hare (roast or) stewed)	45	4 5	Guinea fowl	136	1 5	Ham	1 500	0 3
Mutton chop (grilled or fried)	90	6	Heart	153	1 5	Kidney	250	0 4
Mutton leg etc (roast boiled or stewed)	68	4	Liver	100	2 5	Meat paste	940	0 25
Pork roast	66	5	Partridge			Smoked pork	1 800	0 15
Pork chops	60	9	Pheasant	100	2	Sausage	1 000	0 25
Rabbit	32	6	Pigeon			Tongue (preserved)	1 870	0 15
Sweetbread	69	3	Turkey	130	1 5			
Tongue (fresh)	79	4	Tripe	72	1 5			
Topside (beef)	50	4	Veal	100	2			
			Venison	86	2			

NOTE

All salted and preserved meats are forbidden

Roasts are best since they contain more calories per mg of sodium content

Meat extracts like Bovril and Oxo are forbidden

The simple meats – beef mutton lamb pork hare and rabbit – are the best Next comes game Of offal sweetbread fresh tongue and liver are best

FISH

Permitted		
Bass	75	1 7
Brill (steamed)	94	1 -
Dabs (fried)	127	2 0
Eels (stewed)	73	5 1
Herring (fried)	101	2 3
Herring s roe fre h (fried)	87	3 0
Mullet	94	1 3
Plaice (fried)	124	1 9
Salmon (fresh)	107	1 9
Sprats (fried)	132	3 4
Trout fre h wat r	88	1 5
Turbot	90	1 1

Doubtful		
Bream (sea)	113	0 88
Cod fried	161	0 87
grilled	110	1 5
steamed	100	0 82
Cod s roe (fried)	127	1 6
Flounder (steamed)	115	0 83
Haddock (steamed)	121	0 80
Hake (steamed)	118	0 90
Hake (fried)	153	1 3
Halibut	110	1 2
Mackerel (fried)	153	1 2
Plaice (steamed)	120	0 77
Pollack (steamed)	95	0 91
Pollack (fried)	162	0 96
Skate (fried)	182	1 3
Sole Do er (fried)	192	1 2
Sole Dover (steamed)	110	0 76
Sole lemon *(fried)*	136	1 6
Sole lemon (steamed)	115	0 78
Whiteba t (fried)	225	2 4
Whiting	127	0 71

Forbidden		
Bloaters	703	0 36
Cockles	3 5 0	0 01
Crab (boiled)	366	0 35
Fish paste	1,480	0 12
Haddock (smoked)	1 2-0	0 08
Kippers	990	0 08
Lobster	325	0 36
Mussels (boiled)	-10	0 41
Oysters	505	0 10
Prawns	1 590	0 06
Scallops	265	0 4
Shrimps	3 840	0 03
Trout (sea)	207	0 63
Whelks	265	0 34
Winkles (boiled)	266	0 37

NOTE

Fish cakes made with any but forbidden fish without salt and fried in olive oil are recommended

FRUIT

Permitted			*Permitted*		
Apples	2	20	Greengages	1 4	34
Apricots	1	30	Oranges	2 9	9
Bananas	1 2	70	Peaches	2 7	13
Blackberries	3 7	8	Pears	2 3	18
Cherries	2 8	16	Pineapple	1 7	29
Currants	2 7	10	Plums	1 7	2-
Dates	4 7	27	Quinces	3 2	8
Figs	1 6	26	Raspberries	- 5	10
Gooseberry	1 -	31	Rhubarb	1 5	2 5
Grapes	1 6	40	Strawberries	1 5	17
Grape fruit	1 4	16			

NOTE

These are average samples of fresh fruits

Doubtful fruits are melon (19 5/1) and passion fruit (30/1)

Stewed fruit is best because of its higher calorific value e g stewed apples (0 1/170)

Tinned fruits in syrup are also good

Dried fruits are less beneficial e g tinned apricots (0 9 62) dried apricots (56/3) Raisins and sultanas at 52/4 7 may be allowed occasionally

Preserved olives (2 250/0 05) are forbidden

equal parts of milk and water Shredded wheat with diluted milk and plenty of sugar is recommended

Milk puddings Milk should be diluted with equal parts of water margarine must not be used

Flour sauces Make without salt and with equal parts of milk and vegetable water Use dripping instead of margarine

Bread Home made bread made with yeast flour lard and milk without salt is allowed

DAIRY PRODUCE AND FATS

Permitted			*Doubtful*			*Forbidden*		
Butter (fresh)	223	3 5	Milk (fresh)	50	1 -	Cheese	600	0 5
Cream cheese (home made)	110	8	Milk (sweet condensed)	143	2	Egg white	192	0 2
Cream	31	13				Margarine	318	0 5
Egg yolk	50	7				Butter (salted)		
Olive oil	0 1	9 290						
Lard	-	450						
Dripping	5	200						
Suet	25	44						

NOTE

Butter may be kneaded in water to reduce its salt content

Home made cream cheese must be made without salt

Dilute milk with half its volume of water

Use olive oil dripping lard or suet in cooking instead of butter or margarine whenever possible

MEAT POULTRY AND GAME

Permitted			*Doubtful*			*Forbidden*		
Roast beef	6-	6	Chicken	80	2	Bacon	1 200	0 3
Grilled steak	67	5	Duck	195	1 5	Beef (silverside)	1 470	0 2
Stewed steak	38	5 5	Goose	145	2	Brains	150	0 7
Hare (roast or) stewed)	45	4 5	Guinea fowl	136	1 5	Ham	1 500	0 3
Mutton chop (grilled or fried)	90	6	Heart	153	1 5	Kidney	-50	0 4
Mutton leg etc (roast boiled or stewed)	68	4	Liver	100	2 5	Meat paste	940	0 25
Pork roast	66	5	Partridge Pheasant Pigeon	100	2	Smoked pork	1 800	0 15
Pork chops	60	9	Turkey	130	1 5	Sausage	1 000	0 25
Rabbit	32	6	Tripe	72	1 5	Tongue (preserved)	1 870	0 15
Sweetbread	69	3	Veal	100	2			
Tongue (fresh)	79	4	Venison	86	2			
Topside (beef)	50	4						

NOTE

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The simple meats – beef mutton lamb pork hare and rabbit – are the best Next comes game Of offal sweetbread fresh tongue and liver are best

Honey (10 7/26) and jam (15 9/16) are recommended
Golden syrup (270/1) chutney (150/1) and mincemeat (200/0 5) are prohibited
Toffee (115/3 5) and black treacle (96/2 5) should be avoided

Beverages

Permitted			*Prohibited*		
Coffee	0 3	15	Bournvita	360	1
Lemonade	0 5	100	Bovril	5 580	0 02
Tea	0 4	2	Cocoa	650	0 7
Beer	15	3	Horlicks	690	0 6
Wine			Marmite	6 130	0 01
Spirits			Ovaltine	249	1 5
			Oxo Cubes	10 600	0 02
			Virol	374	1

Condiments

Permitted			*Prohibited*		
Ginger	34	7 5	Curry	450	0 5
Mustard	5	90	Salt	38 500	0
Pepper	7	45			
Vinegar	20	0 2			

Note

Since so small a quantity of curry is required to flavour a dish it may be allowed despite the adverse figures shown

Cakes Pastries and Puddings

Permitted			*Doubtful*			*Forbidden*		
Apple dishes	50	4	Biscuits	150	3	Cakes	150–500	2–3
Blancmange	45	2 5	Buns	120	3			
Cereal puddings (rice etc)	50	3	Cheese cake	138	3	Dumpling	488	0 5
Custard	50	2	Jam roll	151	2 5	Gingerbread	336	1
Doughnuts	60	6	Rock cakes	150	3	Mince pies	225	1 5
Fruit custard	30	3	Tarts	150	3	Pastries	250	2
Fruit tarts	76	3				Puddings	100–250	1–3
Jelly	8	9 5				Scones	170	2
Milk jelly	33	3				Swiss roll	650	0 4
Pancake	88	4				Yorkshire pudding	412	0 5
Shortbread	86	6						
Sponge cake	79	4						
Trifle	50	3						

Note

Oatmeal biscuits are allowed if made without salt and with lard instead of butter or margarine
Cereal puddings should be made with diluted milk and without margarine
Yorkshire pudding is permissible if made without salt

General Rules

No free salt or ordinary salt substitutes no salt in cooking Sodium free salt substitutes usually made with potassium such as neo seleron are permitted
No foods made with baking powder
No medicines containing sodium
No preserved salted smoked or tinned foods (except dried and tinned fruit)
Dilute milk with half *its volume of water*

Use dripping lard olive oil or suet instead of butter or margarine wherever possible

Supply calories chiefly with selected cereals cream fat fresh meat, potatoes sugar sweets fruit and nuts

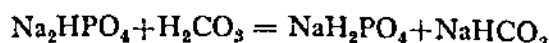
Avoid bread biscuits certain cereals margarine salted butter cheese bacon ham tongue sausages meat extracts shell fish fish paste milk beverages cakes and pastries

Fluid should be encouraged but few patients feel like drinking much if they are adhering to the diet faithfully

Cation exchange resins are synthetic insoluble macromolecular organic compounds in powder form which when suspended in a solution behave like electrolytes acid resins exchange hydrogen ions for any other cation in the solution but prefer calcium potassium or sodium in that order In 1946 Dock pointed out that such resins would absorb sodium from the gut and since then they have gradually found their place as adjuncts to the mercurial diuretics and the low sodium diet (Dock and Frank 1950) At the present time the most effective and readily available cation exchange resin for therapeutic purposes is probably carbo resin (Lilly) Two thirds of the 88 per cent cation exchange fraction of this resin is in the carboxylic acid form one third in the form of its potassium salt In the human gut each gramme of carbo resin is capable of absorbing 1 meq (23 mg) of sodium and passing it out in the fæces when the patient is taking about 1 5 Gm of sodium per day If the dose is 15 Gm suspended in water three times a day 1 Gm of sodium should be removed daily in this way The amount of sodium absorbed by the resin is proportional to the quantity of sodium in the diet Thus with a 0 5 Gm low sodium diet 1 Gm of resin absorbs only 0 3 meq of sodium on a 3 Gm low sodium diet it may absorb as much as 2 meq Undue loss of potassium presents no problem with this resin but calcium deficiency may arise if treatment is prolonged As a rule, however patients do not like taking resins and they are mostly used intermittently as a protection against unavoidable or wilful dietetic indiscretions or liberties—e g while on holiday Neither potassium nor calcium should be given at the same time as the resin or it will absorb less sodium and if there is constipation which is a common complication of resin therapy, it should not be relieved by magnesium salts for the same reason

Carbonic anhydrase inhibitors

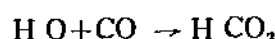
Conservation of body base and excretion of acid is partly achieved by the distal tubules where sodium alkaline phosphate interacts with carbonic acid to form acid phosphate and bicarbonate



$$Na_2HPO_4 + H_2CO_3 = NaH_2PO_4 + NaHCO_3$$

The acid phosphate is excreted and the bicarbonate reabsorbed so that half the sodium is saved This reaction is helped by an anzyme carbonic

anhydrase which accelerates the formation of carbonic acid from CO and water



$$H\ O + CO \rightarrow H\ CO_3$$

If the formation of H CO_3 were to be suppressed alkaline phosphate would be excreted as such and sodium would be no longer conserved

In 1940 Mann and Keilin identified sulphanilamide as a specific inhibitor of carbonic anhydrase and after further research Roblin and his colleagues found that of all the active heterocyclid sulphonamides diamox was the most promising in this respect (Miller *et al* 1950) It is rapidly absorbed and is excreted unchanged by the kidney in 6 to 12 hours A single oral dose of 250 mg is sufficient to interfere with the chain of events outlined above so that the tubules experience difficulty in reabsorbing sodium

In clinical practice however diamox in doses of 250 mg daily has so far proved disappointing and certainly the weakest of the four methods of relieving the body of sodium

Combined low sodium regime

With these four weapons adequate control of the sodium balance is not at all difficult The art is to find the best combination for each particular patient and the danger is the low salt syndrome first described by Shroeder (1949) The most powerful of the four is the diet and if patients will only abide by it absolutely the other three methods may usually be withheld altogether moreover patients tend to lose their taste for salt if they resolutely refuse to titillate it If patients prefer a 2 or 3 Gm sodium diet they will certainly need weekly injections of mersalyl or thiomerin daily merchloran if they can tolerate it or fairly heavy doses of a potent cation exchange resin diamox alone is rarely strong enough to hold the situation in check Patients who do not mind the diet for the most part but who insist on occasional breaks can have these lapses adequately covered by a mercurial diuretic or resin

The low sodium regime has revolutionised the treatment of heart failure and is a great deal more effective than digitalis except in cases of auricular fibrillation with rapid ventricular rate It is also just as successful in isolated left ventricular failure as in congestive heart failure or pure right ventricular failure It has the triple value of combatting œdema itself reducing the blood volume and venous pressure and so improving the function of the overloaded heart and relieving pulmonary venous congestion whether due to heart failure or mitral stenosis

Aminophylline

Aminophylline (theophylline ethylenediamine) benefits cases of heart failure in four different ways (1) it lowers the venous pressure promptly and thereby relieves both left and right ventricular failure (2) it is an excellent bronchial antispasmodic and therefore particularly helpful in

cor pulmonale (3) it is a powerful respiratory stimulant acting reflexly by way of carotid sinus chemoreceptors and abolishes Cheyne-Stokes breathing as first recognised by Vogl (1927 1942) (4) to some extent it appears to be a cardiac tonic, for it makes the heart beat more strongly There is no evidence that it improves the cerebral circulation (Wechsler, Kleiss and Kety 1950) and direct measurements of coronary blood flow in man by means of coronary sinus catheterisation do not support the belief that aminophylline is a coronary vaso dilator (Foltz *et al* 1950)

The drug may be given intravenously in doses of 0 25 to 0 5 Gm in cases of paroxysmal cardiac dyspnœa or pulmonary œdema with dramatic results it should be injected slowly in order to avoid overstimulating respiration Unfortunately aminophylline is often very painful when given intramuscularly owing to its high pH although preparations are on the market for use by this route

Orally aminophylline causes severe dyspepsia if given in effective doses the usual 0 1 Gm tablet three times daily after meals being far too small Some attempts have been made to overcome this difficulty perhaps the best preparation so far being theodrox (Riker) in which 0 2 Gm of aminophylline is combined with 4 gr of dried aluminium hydroxide gel taken four hourly 0 2 Gm of aminophylline is an adequate dose and theodrox is relatively well tolerated

An aminophylline suppository of 0 4 Gm at night will prevent both Cheyne Stokes breathing and paroxysmal nocturnal dyspnœa and in doing so may earn the patient s thanks for a good night s sleep

Etophylate a preparation in which theophylline ethanoic acid is combined with diethylenediamin (piperazine) has the great advantage of having a pH around 7 and is therefore non irritant moreover it is freely soluble and stable while retaining the therapeutic properties of theophylline It may be given orally in doses of 0 5 Gm three times daily and is painless if injected intramuscularly in similar dosage

Choline theophyllinate may also be taken by mouth in doses of 0 3 to 0 5 G t d s without fear of gastric disturbance but since the pH of a 0 8 per cent aqueous solution is 9 7 it is unsuitable for intramuscular injection

Oxygen is of little value in heart failure except in the following circumstances (1) in anoxic cor pulmonale (2) when acute bronchitis or bronchopneumonia has precipitated or complicated heart failure from other causes (3) in massive pulmonary embolism (4) in acute pulmonary œdema (5) in rare cases of heart failure occurring in cyanotic forms of congenital heart disease and (6) in acute cardiogenic shock from cardiac infarction

Acupuncture When œdema is gross and fails to respond to the measures previously outlined it may be necessary to resort to acupuncture A triangular cutting needle is used and about a dozen punctures are made in each leg the patient is then seated in a chair with his legs in a tub To facilitate drainage the legs may be swabbed down with warm citrate solution from time to time Due antiseptic precautions must be maintained Fluid

may continue to exude for twenty four to forty eight hours and it is not uncommon for the total quantity to be measured in gallons Southey s tubes constitute a cleaner way of removing fluid on the same principle Several large bore needles are inserted into the subcutaneous tissues of the thighs or calves and fluid is allowed to drain away through attached rubber tubes into a container

Relatively little protein but a lot of sodium is lost by this method and the good effect is not merely cosmetic on the contrary, the blood volume diminishes the venous pressure falls the cardiac output may pick up and spontaneous diuresis may follow

Attacks of paroxysmal cardiac dyspnœa or of acute pulmonary œdema are treated by methods designed to lower the venous filling pressure as quickly as possible and so to reduce the output of the right ventricle The sitting position will usually have been adopted already by the patient Morphine ¼ to ⅓ of a grain (15 to 20 mg) intramuscularly or ⅙ of a grain (10 mg) intravenously depresses the excited respiratory reflexes and soothes the patient Pethidine 50 to 100 mg intramuscularly may be equally effective Venous tourniquets may be applied round the thighs to trap blood in the legs or venesection may be preferred Theophylline ethylene diamine (aminophylline) 0 24 to 0 48 G intravenously lowers the venous pressure immediately relieves bronchial spasm and may have a direct stimulating action on the heart (fig 7 02) Tetraethylammonium bromide 200 to 300 mg intravenously is a useful agent for lowering venous pressure and may relieve attacks quickly (Hayward 1948) Hexamethonium bromide 20 to 30 mg or pentapyrrolidinium bitartrate (ansolysen) 5 mg subcutaneously may be equally effective

Digoxin and strophanthin are probably best avoided in view of their pressor actions indeed paroxysmal cardiac dyspnœa may occasionally be initiated by intravenous digoxin

Oxygen is of little value in paroxysmal cardiac dyspnœa for the arterial oxygen saturation is normal but may be given with advantage in acute pulmonary œdema Nikethamide is contraindicated, for the aim is to depress respiration not to stimulate it Adrenaline is dangerous in ischæmic cases because it may provoke angina pectoris paroxysmal ventricular tachycardia or ventricular fibrillation but it may be given in doses of 0 5 mg subcutaneously to relieve bronchial spasm in hypertensive cases (Platz 1947) Atropine should be avoided, for it has no therapeutic value and causes unnecessary tachycardia

Dramatic results may follow treatment directed against *the cause of the underlying heart disease* This applies particularly to cases of thyrotoxicosis anæmia beri beri arterio venous aneurysm severe pulmonary stenosis large patent ductus atrial septal defect mitral or aortic stenosis and primary abnormalities of rhythm and to a lesser extent to bronchitis and asthma active syphilitic aortitis bacterial endocarditis and any form of systemic hypertension

If in spite of all these measures, heart failure continues an attempt may be made to reduce the oxygen requirement and therefore the work of the heart by means of antithyroid drugs *or total ablation of the thyroid gland* (Blumgart Levine and Berlin 1933) The former is preferable because the treatment can be abandoned if unsuccessful (Bedford 1949) Relatively large doses are necessary usually 0 2 to 0 3 Gm of propyl thiouracil daily It must be admitted however that results are far from satisfactory Radioactive iodine offers another means of inducing artificial myxoedema (Blumgart *et al* 1950)

Ligation of the inferior vena cava below the renal veins may be tried in obstinate cases (Cossio 1952) The surgical mortality is about 6 per cent and in at least half the cases initial improvement has been maintained for months or years The operation lowers the central venous pressure Œdema tends to clear rather than increase The chief complication is recurrent phlebothrombosis in the legs

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( ) Fac es (note bilateral iridectomy)



(b) Showing h gh arched palate and deformed teeth



(c) Spider fingers

Fig 8 01—A case of arachnodactyly

This patient was 6 ft h gh and also showed hypotonia scoliosis and flat feet



FIG 8 02—Hyperteleorism in a case of pulmonary stenosis with reversed interatrial shunt

CLASSIFICATION

It has been customary to divide congenital heart disease into acyanotic and cyanotic forms and to subdivide the latter into types with permanent cyanosis (morbus cœruleus or blue babies) and types with late terminal or transient cyanosis (cyanose tardive). This has never proved entirely satisfactory and a new classification is therefore offered It was based originally on a series of 200 proved clinical cases (Wood 1950) and takes function into account The series has since increased to 900 and the relative incidence of each type is now given in the table These figures do not apply to infants many of whom die during the first year of life

NO SHUNT					
GENERAL	*per cent*	LEFT SIDED	*per cent*	RIGHT SIDED	*per cent*
Dextrocardia	0 5	Aortic atresia	rare	Ebstein's anomaly of the tricuspid valve*	1 0
Familial cardiomegaly	rare	Aortic hypoplasia	0 5		
Friedreich's disease	rare	Aortic incompetence	0 5		
Gargoylism	rare	Aortic rings	rare	Idiopathic dilatation of the pulmonary artery	1 0
Heart block	1 5	Aortic stenosis	3 0		
Von Gierke's disease	rare	Coarctation of the aorta	9 0	Pulmonary stenosis (isolated)	
		Cor triatriatum	rare		
		Fibroelastosis	rare	intundibular	2 0
		Left coronary artery arising from pulmonary artery	rare	valvular	10 0
		Mitral stenosis	rare		
		Right sided aortic arch (isolated)	rare		
Total	2 0	Total	13 0	Total	14 0

* Some cases are cyanotic

WITH SHUNT

ACYANOTIC LEFT TO RIGHT SHUNT (pulmonary plethora)	per cent
Left ventricular enlargement	✓
✓Patent ductus	13 0
Aorto pulmonary septal defect	0 3
Right ventricular enlargement	✓
Atrial septal defect	18 0
A S D with pulmonary stenosis	2 0
Anomalous pulmonary venous drainage (partial)	
Enlargement of both ventricles	✓
Ventricular septal defect	8 0
V S D with pulmonary stenosis	1 3
Miscellaneous 3 7 per cent	
Total	4 6

CYANOTIC RIGHT TO LEFT SHUNT	per cent
DIMINISHED PULMONARY BLOOD FLOW	
NORMAL OR LOW P A PRESSURE	
Left ventricular enlargement	
Tricuspid atresia ✓	1 5
Anomalous drainage of S V C or I V C into left atrium	rare
Single ventricle with pulmonary stenosis	rare
Right ventricular enlargement	✓
Fallot s tetralogy	11 0
Pulmonary atresia	1 7
Pulmonary stenosis with reversed interatrial shunt	3 0
HIGH P A PRESSURE	
Pulmonary hypertension with reversed shunt	
i Patent ductus	2 0
ii Ventricular septal defect (Eisenmenger s complex)	3 0
iii Atrial septal defect	1 5
Cor triloculare biatriatum*	rare
INCREASED PULMONARY BLOOD FLOW	
Transposition of the great vessels	1 0
Persistent truncus	rare
Total anomalous pulmonary venous drainage into S V C or R A	rare
Cor biventriculare triloculare	rare
Total	24 7

* Some cases may have pulmonary plethora

DEXTROCARDIA

Mirror image dextrocardia is usually but not invariably associated with complete transposition of the viscera The heart is functionally and structurally healthy The electrocardiogram for obvious reasons shows reversal of all complexes in lead 1 with leads 2 and 3 interchanged (fig 8 03)

The diaphragm is always lower on the cardiac side of the chest its position not being influenced by the location of the liver or stomach

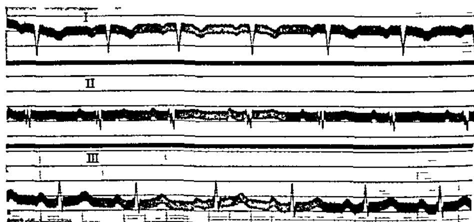


Fig 8 03—Electrocardiogram showing reversal of all complexes in lead I while lead II and III are interchanged

IDIOPATHIC HYPERTROPHY OF THE HEART

Under this heading in the past were grouped a heterogenous collection of cardiopathies in infancy which bore little or no relationship to one another and which for the most part have since been defined in more precise terms The group included examples of von Gierke s disease anomalous left coronary artery arising from the pulmonary artery isolated myocarditis thyroid deficiency nutritional cardiopathy in infants born of diabetic mothers and fibroelastosis Nothing would be gained by discussing idiopathic hypertrophy as an entity in itself

FAMILIAL CARDIOMEGALY

From time to time cases of cardiac enlargement are encountered in young subjects for which there is as yet no adequate explanation They are prone to paroxysmal tachycardia and atrial fibrillation and on examination there is often diastolic gallop X rays show considerable cardiac enlargement particularly of the left ventricle (fig 8 04) Left bundle branch block is usually found These patients are apt to die suddenly presumably from ventricular fibrillation or by degrees from congestive heart failure when still relatively young

Some of these cases appear to have a familial basis (Addarii *et al* 1946 Evans 1947 and 1949) Necropsy reveals myocardial fibrosis and compensatory hypertrophy of muscle Von Gierke s disease isolated myocarditis nutritional cardiopathies Friedreich s disease and abnormal coronary vessels must be excluded



Fig 8 04—Unexplained cardiac enlargement in a relatively young man (there was also left bundle branch block)

FRIEDREICH'S ATAXIA

Cardiac manifestations associated with Friedreich's ataxia were first noted in five of six cases reported by Friedreich himself in 1863 Degeneration of muscle fibres interstitial fibrosis and compensatory hypertrophy of remaining muscle are the usual pathological findings the left ventricle being chiefly involved and the picture being not unlike that of familial cardiomegaly

In the majority there are no cardiac symptoms but the electrocardiogram may show flat or inverted T waves chiefly in antero lateral left ventricular surface leads or their equivalents or bundle branch block (Evans and Wright 1942) In a minority there are paroxysmal rhythm changes usually atrial tachycardia or fibrillation and occasionally there is fatal congestive heart failure (Russell 1946)

CONGENITAL HEART BLOCK

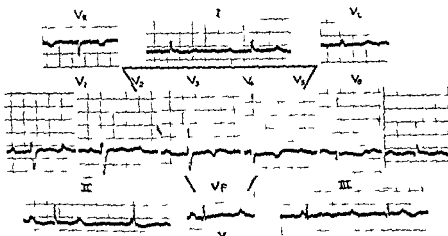
It has long been thought that congenital heart block was related to ventricular septal defect the association being accepted in 30 out of 44 cases reviewed by Yater Lyon and McNabb (1933) four of them proved at necropsy At that time however ventricular septal defect was diagnosed far too readily (Wood *et al* 1954) and there is little doubt that the

relationship has been over emphasised Thus routine electrocardiography in 200 cases of ventricular septal defect seen by Brown (1950) did not reveal heart block in a single instance In a personal series of 72 cases of isolated ventricular septal defect proved by modern methods heart block occurred only once and in 162 cases in which ventricular septal defect was associated with other anomalies it also occurred only once Conversely ventricular septal defect was not present in 13 out of a consecutive series of 15 cases of congenital complete heart block although it had been diagnosed previously in several of them

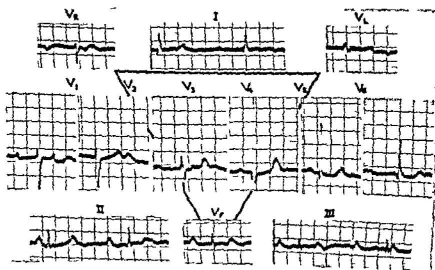
Congenital heart block is complete and permanent twice as often as it is partial or variable (Aitken 1932) Although congenital complete heart block does not differ radically from acquired heart block (q v) it has several characteristic features of its own

1. It is present from birth and rarely may be familial (Wendkos and Study 1947)
2. The resting ventricular rate is usually faster averaging 50 beats per minute (range 36 to 80)
3. The rate commonly increases by about 33 per cent after a subcutaneous injection of atropine gr 1 75 (Aitken 1932) or on effort (Campbell and Suzman 1934)
4. In view of the faster rate and its increase on exercise effort tolerance may be almost normal and the heart but little enlarged
5. Stokes Adams fits are rare according to Brown (1950) although Janet Aitken (1932) tabulated syncopal attacks of unspecified nature in 18 per cent of the 39 cases she reviewed None of my own series of 15 cases has had a Stokes Adams seizure and only one of the eight described by Campbell and Suzman (1934) had genuine attacks It should be remembered that heart block may be acquired in cases of congenital heart disease including ventricular septal defect and Stokes Adams fits may certainly occur then as in the case reported by Rogers and Rudolph (1951)
6. A functional mitral diastolic murmur due to the large mitral stroke blood flow was heard in over three quarters of the present series particularly when the rate was under 50 and was accentuated when the atria contracted synchronously with the period of rapid ventricular filling it should not be misinterpreted as evidence of active rheumatic valvulitis
7. The QRS complex of the electrocardiogram is normal bundle branch block complexes at once suggesting an acquired lesion Inverted T waves in antero lateral chest leads over the left ventricle are not necessarily sinister in congenital heart block and may become upright on exertion (fig 8 05)

The prognosis of uncomplicated cases of congenital complete heart block is believed to be good if the ventricular rate is over 50 and still fairly



(a) At rest showing inverted T waves in chest leads



(b) After effort the rate is unchanged but the T waves are now upright

Fig. 805 —Congenital heart block with a ventricular rate of 48 beats per minute

good if the rate is between 40 and 50 The oldest in the present series was 39 and two of the others were over 30 Sudden unexpected deaths have occurred however and perhaps one should be a little guarded

Treatment when necessary is the same as for acquired cases but is rarely indicated

VON GIERKE'S DISEASE

General enlargement of the heart sooner or later resulting in sudden death or congestive failure may be due to glycogen storage in the myocardial muscle fibres as well as in the liver, kidneys and other organs (Von Gierke 1929) Although few cases survive childhood Von Gierke's disease has been reported occasionally in adults even as late as the fifth decade It is characterised by hepatomegaly retardation of growth and sexual development persistent ketosis with acetonuria hypercholesterolæmia raised blood glycogen (normal 12-20 mg per cent) low fasting blood sugar and a flat blood sugar curve following the subcutaneous injection of 0 25 to 0 5 mg of adrenalin due to failure of mobilisation of glycogen (Ellis and Payne 1936 Crawford 1946) Some cases are familial When the heart is involved microscopy reveals heavily vacuolated muscle fibres which when specially stained are seen to be filled with glycogen It is believed that Von Gierke's disease is due to deficiency of one or more of the enzymes such as liver phosphatase that are indispensable to the breakdown of glycogen to glucose (Cori 1952)

GARGOYLISM

Another rare congenital metabolic disorder involving the heart is gargoylism Here there is a widely distributed abnormal storage of a macromolecular glycoprotein in parenchymal fibroblastic and other connective tissue cells (Lindsay 1950) Gargoyles are mentally retarded, large headed pot bellied dwarfs with deep guttural voices deafness coarse heavy features large tongues abundant hair and other skeletal peculiarities Of 26 cases in the literature the heart was involved in 85 per cent (Emanuel 1954) There was usually interstitial myocardial fibrosis and thickening of the valves—chiefly the mitral less frequently the aortic sometimes the tricuspid and rarely the pulmonary (as in rheumatic heart disease) Many of the cases died from heart failure

FIBROELASTOSIS

One of the relatively common causes of sudden death or rapidly fatal congestive heart failure in infancy is what is now termed fibroelastosis Affected infants may appear to be normal at birth, but within a few weeks or months suddenly develop attacks of dyspnœa and cyanosis due to acute left ventricular failure and either die suddenly in an attack or more gradually in a state of congestive failure (Adams and Katz 1952) The condition may occur alone or in conjunction with coarctation of the aorta aortic stenosis aortic atresia or mitral stenosis and is characterised by enlargement of the left ventricle *overlying a uniformly thick dense white* endocardium Bonham Carter (1955) has stressed its association with

hyperteleorism Good descriptions include those of Gross (1941) Prior and Wyatt (1950) and Dennis *et al* (1953)

Many of the instances of idiopathic hypertrophy of the heart reported in the older literature were undoubtedly of this nature including the critical eighth case of Kugel (1939) which was proved not to be due to glycogen storage The pathology is not yet fully understood Fœtal endo carditis was discarded by Gross (1941) A developmental defect is more probable The thickening appears to be embryonic myxomatous tissue richly supplied with elastic fibres (Glynn and Reinhold 1949) Johnson (1952) makes a good case in favour of its being due to anoxia, and describes various ways in which this might be brought about in utero including temporary closure of the foramen ovale during the development of the interatrial septum and premature closure of the foramen ovale before birth Anoxia might well be responsible for fibroelastosis in cases of anomalous left coronary artery arising from the pulmonary artery and aortic atresia with closed interventricular septum it would also explain fibroelastosis of the left atrium in cases of mitral atresia and of the right ventricle in cases of pulmonary atresia with closed interventricular septum

ANOMALOUS CORONARY ARTERIES

A *single coronary artery* arising from the aorta may follow the normal course of the left or right coronary artery divide early into a left and right coronary artery or take an altogether atypical course with more or less equal frequency (Smith 1950) The majority of those in which the course has been normal have been found by chance in adults their average age being 45 and the oldest 80 Cardiac function is usually normal The majority of those in which the single vessel has taken an atypical course have been associated with other serious cardiac anomalies and have died in infancy

When *the left coronary artery arises from the pulmonary artery* it is set the impossible task of perfusing a high pressure chamber by means of the pulmonary artery pressure which is only about 15/7 mm Hg moreover the perfusing blood is only about 70 per cent saturated with oxygen Although the high pressure gradient between right and left coronary artery must encourage anastomotic flow this is rarely sufficient to meet the needs of the left ventricle In consequence that chamber degenerates necrosed muscle fibres may calcify surviving muscle hypertrophies the endo cardium becomes fibroelastotic and the heart weight averages four times the normal (Kaunitz 1947) Clinically infants may suffer from attacks of breathlessness and peripheral cyanosis due to left ventricular failure especially when suckling angina pectoris which is not always recognised in infants may cause great distress (Bland White and Garland 1933) and sudden death is the rule The left lower lobe is not infrequently collapsed by the huge left ventricle About three quarters of all cases reported have

died in infancy usually between the third and twelfth month but a quarter have reached adult life the average age of death then being 37 years (range 17 to 64) In this small group the right coronary artery has been large and seems to have supplied both ventricles

When *the right coronary artery arises from the pulmonary artery* the situation is not the same for the right ventricle works at low pressure and is therefore much more easily perfused The left coronary artery is able to meet the demands of the base of the left ventricle posteriorly chiefly through its left circumflex branch There are usually no clinical manifestations cardiac function being normal and the anomaly is only discovered incidentally at necropsy A typical case reported by Cronk Sinclair and Rigdon (1951) died at the age of 90

COARCTATION OF THE AORTA

The word coarctation comes from the Latin *coarctatus* meaning pressed together tightened or contracted As applied to the aorta it means a stricture of the arch usually just below the origin of the left subclavian artery

Embryology It will be recalled that on each side there are two primitive aortas each having a ventral and a dorsal part joined by an arch These three parts are called respectively the ventral aorta the dorsal aorta and the first aortic arch In front the two ventral aortas fuse to form a single tube from which develops the primitive heart the truncus arteriosus and the common ventral aorta The two dorsal aortas also fuse between the fourth thoracic and fourth lumbar segments forming a single trunk the common dorsal or descending aorta Caudal to the first pair of aortic arches spring five other pairs the six corresponding to the six branchial arches (fig 8 06a) In fishes these six vascular arches persist and supply the gills with blood for oxygenation

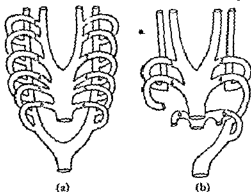


Fig 8 06 (a)—The six primitive aortic arches (b) Subsequent arrangement of the six primitive aortic arches in man (see text)

In man and mammals subsequent development is illustrated in figure 8 06b The first second and fifth arches disappear The third becomes the common carotid artery the external carotid springing from it anteriorly the internal linking up via the cranial portion of the dorsal aorta The fourth arch becomes the proximal part of the subclavian artery on the right side and the final aortic arch proximal to the junction of the ductus arteriosus on the left The sixth pair of arches is separated from the

aortic system by the aorto pulmonary septum which divides the truncus into anterior and posterior halves the anterior half becomes the ascending aorta the posterior the pulmonary artery The division of the truncus extends cranially to a point just beyond the anterior ends of the sixth pair of arches the mouths of which are included in the posterior section and therefore in the pulmonary system On the right side the sixth arch becomes the right pulmonary artery and loses its connexion with the right dorsal aorta on the left it becomes the left pulmonary artery and preserves its connexion with the left dorsal aorta in the form of the ductus arteriosus While these changes are going on harmonious alterations take place in the ventral and dorsal aortas In front the two ventral aortas fuse into a single ascending aorta as already indicated Behind the dorsal aortas undergo considerable modification the upper part forms a portion of the internal carotid artery as previously described the segment between the third and fourth arches disappears caudal to the fourth arch the dorsal aorta disappears on the right side except for that part of it which is incorporated in the right subclavian artery and forms the posterior part of the aortic arch on the left side The left subclavian artery links up with the left dorsal aorta just below the junction of the sixth arch i e just below the ductus

Many anomalies may result from faulty development of this aortic system Thus, the caudal part of the right dorsal aorta may persist so that there are two aortic arches or the caudal part of the left dorsal aorta may disappear in favour of the right so that the final aortic arch is right sided The most important however is partial obliteration of that part of the left dorsal aorta which lies between the fourth and sixth arches i e just above the ductus or between the sixth arch and the point of fusion of the two dorsal aortas i e just below the ductus This short segment of the aorta is often called the isthmus on account of the frequency with which it is narrowed but in coarctation or isthmus stenosis narrowing is extreme and often remarkably abrupt There are said to be two main types infantile and adult (Bonnet 1903) In the former (fig 8 07a) the constriction is above the ductus which remains patent and carries venous blood to the descending aorta it is incompatible with more than a few years of life In the latter (fig 8 07b) the ductus is closed or if patent the constriction is below it so that it plays no part in compensating for the defect Aortic atresia with a patent ductus

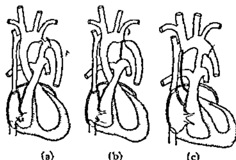


Fig 8 07—Diagrams illustrating the three main types of coarctation of the aorta
(a) Infantile type with patent ductus feeding the descending aorta
(b) Common adult type
(c) Aortic atresia with patent ductus feeding the whole systemic circulation

feeding the whole systemic circulation (fig 8 07c) constitutes a third type (Bramwell 1947) but such cases all die in infancy Other variants of these three main types have been described by Evans (1933)

This simple anatomical classification however is no longer satisfactory for it does not tally with the physiological facts and is of little practical help to the surgeon In the first place the pressure in the descending aorta is maintained by *blood flowing into the aorta from collateral channels and* by the peripheral vascular resistance not by the small quantity of blood passing through the stricture thus it is not altered by obliterating the coarctation altogether Secondly if a patent ductus joins the aorta below the stricture blood ordinarily flows from aorta to pulmonary artery as in the adult type with patent ductus for the pressure in the descending aorta is far higher than that in the pulmonary artery even when the stricture is totally occluded. In a typical case of this sort investigated by the author the pressure was 150 90 in the brachial artery 95 80 in the descending aorta and 45 27 in the pulmonary artery The catheter was passed through the ductus and emerged into the descending aorta below the coarctation The shunt was undirectional from aorta to pulmonary artery samples from the right brachial artery and descending aorta were 95 and 93 per cent *saturated with oxygen respectively the pulmonary blood flow was 12 litres* per minute or about twice the systemic flow When a patent ductus joining the aorta below the stricture actually supplies the descending aorta with venous blood it can only do so because the pulmonary vascular resistance is equal to or greater than the systemic resistance i e about eight times higher than normal This occurs in 10 to 15 per cent of all cases of patent ductus and is an essential part of the Eisenmenger syndrome (q v) but it is not due to the coarctation Bonnet s infantile type of coarctation therefore becomes pulmonary hypertension with reversed aorto pulmonary shunt with coincidental coarctation of the aorta above the ductus It is also undesirable and unhelpful to include aortic atresia in any classification of coarctation of the aorta *for it is an entirely separate* entity On the other hand the site of the stricture is of the greatest importance It is proximal to the left subclavian artery in about 2 per cent of cases (Abbott 1928 Reifenstein *et al* 1947) and low usually below the diaphragm in about 2 per cent (*vide infra*)

In *presubclavian coarctation* the left arm may be under developed palpable collateral vessels and rib notching if present occur only on the right side and X rays do not show *the elongated shadow of a dilated left* subclavian artery above the aortic knuckle The anatomical arrangement can be seen clearly with the aid of angiocardiography or retrograde aortography via the right radial artery Such cases have so far been considered unsuitable for surgical repair

Low coarctation comprises a small group of cases in which the stricture is in the descending thoracic aorta well below the usual site or in the abdominal aorta above or below the renal arteries The group probably

includes cases of local arteritis including periarteritis and that form which has been described in young women usually under the title pulseless disease or Takayasu s disease (Caccamise and Whitman 1952) A short segment of the aorta is thickened and indurated and its lumen greatly reduced The history and subsequent course with the development of similar lesions in major peripheral arteries especially the subclavians reveal the true nature of such cases At least one of the two cases described by Bahnson *et al* (1949) seemed to be of this type and one of four abdominal coarctations in my own series is probably inflammatory (also in a young woman) But true congenital coarctation of the abrupt type can certainly occur below the diaphragm as in the 12 year old girl with hypertensive heart failure described by Kondo and his colleagues (1950) The distinguishing clinical features of low coarctation include a coarctation murmur best heard over the lumbar spine or anteriorly through the abdominal wall no palpable collateral vessels rib notching which is either absent or limited to the last two or three ribs and a normal or unfolded aortic arch radiologically Hypertension has been present in nearly all cases reported but the lesion has usually been above or has involved the renal arteries Surgical repair should be undertaken if technically feasible

A second anatomical point of practical importance is whether the coarctation is elongated or abrupt for this may determine whether or not a graft is necessary

Then if associated congenital anomalies are to be taken into account mitral stenosis fibroelastosis bicuspid aortic valve aortic incompetence and aortic stenosis each deserves as much consideration as patent ductus (*vide infra*) The commonest cause of death from coarctation in infancy for example is left ventricular failure from fibroelastosis (Bonham Carter 1955) this combination therefore has more justification to be entitled the infantile type of coarctation than Bonnet s type with a patent ductus

On the whole therefore coarctation of the aorta might be better classified quite simply according to its site nature and associated anomalies thus

CLASSIFICATION

SITE	NATURE	ASSOCIATED ANOMALIES
1 Presubclavian	Abrupt	1 Fibroelastosis
2 Isthmus	Elongated	2 Bicuspid aortic valve (Aortic incompetence)
3 Lower dorsal	Hooked	3 Aortic stenosis
4 Subphrenic		4 Patent ductus (with) i Direct shunt ii Reversed shunt
		5 Mitral stenosis

Hæmodynamics The clinical features of the adult form of coarctation depend upon the mechanical effect of the constriction and upon the development of an extensive collateral circulation Much use is made of the branches of the subclavian artery e g the superior intercostal and the internal mammary with its intercostal superior epigastric and musculo phrenic rami also of the thoracic and subscapular branches of the axillary artery These vessels link up with the intercostal branches of the descending aorta and with the inferior epigastric branches of the femoral arteries and so by pass the constriction The blood pressure is elevated in vessels arising from the aorta above the isthmus below it the pulse pressure is much reduced systolic and diastolic pressures oscillating gently around a mean which is nearly always well below the mean brachial pressure (fig 8 08) but which may be slightly raised normal or low compared with

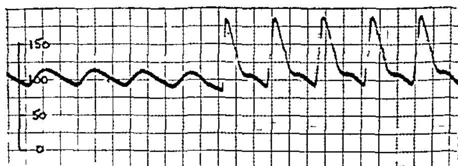


Fig 8 08—Femoral and brachial pressure pulses in a case of coarctation of the aorta

average normal controls The cause of the hypertension is uncertain A raised mean pressure in the legs does not support the mechanical hypo thesis Renal ischæmia was blamed by Rytand (1938) on the grounds that hypertension was only produced experimentally when the aorta was con stricted above the origin of the renal arteries according to Friedman Selzer and Rosenblum (1941) the renal blood flow is appreciably reduced in coarctation although glomerular filtration is normal In acute experiments in dogs the mean pressure in the legs is always reduced (Gupta and Wiggers 1951)

Incidence

Coarctation occurred in 9 per cent of a personal series of 900 cases of congenital heart disease It is said to be 4 to 5 times more frequent in men than in women (Abbott 1928 Reifenstein *et al* 1947) but the ratio was only 2 to 1 in the author s series and also in the 270 cases seen by Gross (1953) The oldest case in the literature died at the age of 92 years (quoted by Abbott 1928) Most cases seen are young adults the anomaly being discovered as *a result of mass radiography About 1 per cent of cases appear*

to be hereditary or familial although very few such instances have been published (Taylor and Pollock 1953) One of my patients for example a married woman of 34 (now 37) had a brother with coarctation who died from cerebral hæmorrhage at the age of 17 and a male cousin with coarctation who died from dissecting aneurysm or aortic rupture at the age of 37

CLINICAL FEATURES

Symptoms

Two thirds of clinical cases are free from all symptoms when first seen They are commonly well developed young men who have experienced no discomfort even on strenuous exercise Minor symptoms include *epistaxis* (6 per cent) *headaches* (6 per cent) or discomfort from *throbbing in the neck* *Migraine* occurs in only 2 per cent despite the frequency of mal formed cerebral vessels *Rheumatism* especially round the shoulder girdle attributed to pressure effects from dilated collateral arteries was mentioned in no less than eight of Bramwell s 26 cases but occurred in only 3 per cent of the author s series despite a routine leading question A history of rheumatic fever was obtained in 5 per cent which is the same as in controls *Intermittent claudication* in the legs occurred in 5 per cent of 212 cases combining the reports of Bramwell (1947) Christensen and Hines (1948) with my own In one instance it interfered seriously with the career of a dancer Although the measured blood flow in the legs is within normal limits at rest (Wakim Slaughter and Clagett 1948) it may not be so on effort and it usually rises after surgical treatment (Bing *et al* 1948) The blood flow in the arms is usually elevated at rest and falls post operatively

Major symptoms are always due to complications and will be discussed later

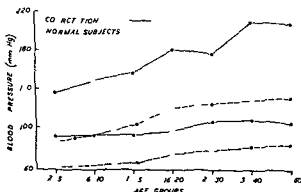


Fig 8 09—Chart showing the relationsh p between blood pressure and age in cases of coarctation of the aorta compared with normal controls

Physical signs

(i) *Excessive pulsation of the carotid arteries* may be visible on inspection

(2) *The blood pressure in the arms* is raised moderately and both systolic and diastolic levels rise gradually with the years much as they do in normal subjects (fig 8 09) There is no vicious circle mechanism because the renal vessels are protected The blood pressure rises sharply on exercise at least during the first few minutes but probably no more than in patients with essential hypertension of similar degree Diminished pulsation in the left subclavian artery may be due to presubclavian coarctation an anomalous vessel or compression from an aortic aneurysm Diminished pulsation in the right subclavian is nearly always due to its having an anomalous origin

(3) The blood pressure in the legs is lower than in the arms in all but the mildest cases Femoral pulsation is poor and at times impalpable (20 per cent) The small pulse is obviously delayed in 95 per cent of cases in which it can be felt Direct arterial tracings reveal a wave form that looks grossly overdamped or not unlike the pattern of a mean arterial pressure (fig 8 08)

In 21 cases investigated by Brown *et al* (1948) at the Mayo Clinic the pressure in the radial artery averaged 196/96, and in the femoral 113/81, whereas in controls they were identical the onset of the femoral pulse was delayed by an average of 0 03 second and the peak by 0 08 second The mean pressure in the femoral artery is usually within normal limits or may be a little low, but it is rarely raised If the femoral arteries were palpated as a routine very few cases of coarctation would be overlooked



Fig 8 10—A visible collateral anastomotic intercostal artery in a case of coarctation of the aorta

(4) *Visible or palpable pulsation of collateral vessels* particularly in the interscapular region posteriorly (fig 8 10) can be demonstrated in about 80 per cent of cases in the age groups usually seen (Christensen and Hines 1949) but is unusual in small children Tortuous and dilated intercostal vessels show up better if the patient bends forward with the arms hanging down—Suzman's sign (Campbell and Suzman 1947)

The *retinal arteries* may be normal tortuous or somewhat constricted but serious hypertensive retinopathy does not occur

Retinal hæmorrhages are seen occasionally however and subhyaloid hæmorrhage may accompany a subarachnoid bleed Papillœdema at once points to a different etiology as was substantiated in two of my cases

The heart itself has all the usual features associated with moderate hypertension (q v) It is hypertrophied rather than dilated and rarely fails in the absence of complications at least under the age of 50 (Reifenstein *et al* 1947) The cardiac output in uncomplicated cases is normal (Bing *et al* 1948) Left ventricular failure in infancy is commonly due to *associated fibroelastosis, and in older children or relatively young adults* to aortic stenosis or incompetence, mitral valve disease other congenital anomalies such as ventricular septal defect and patent ductus or bacterial endocarditis (*vide infra*)

Auscultation

In uncomplicated cases an *aortic systolic murmur* often initiated by an ejection click is usually heard at the apex and base

In practically one third of my cases a *mitral diastolic murmur* was heard at the apex indistinguishable in timing pitch intensity and duration from the Carey Coombs murmur of active rheumatic carditis (Wood 1950) In arriving at this figure of 33 per cent three cases of rheumatic mitral stenosis and five cases in which turbulence could have been due to an excessive mitral blood flow (three with patent ductus and two with ventricular septal defect) were excluded It is inconceivable that a murmur heard so frequently could have been due to active rheumatic valvulitis although this was believed to be the explanation in one instance the erythrocyte sedimentation rate was practically never raised subacute rheumatism rheumatic fever or chorea past or present was no more frequent than in controls (5 per cent) and the incidence of rheumatic mitral stenosis in adults with coarctation was only 2 per cent A similar murmur may be heard in congenital aortic stenosis and in both conditions slight thickening of the mitral cusps due to minor fibroelastotic changes provide a possible though purely speculative explanation The murmur may or may not disappear after successful surgical treatment

The third important murmur of uncomplicated coarctation is heard posteriorly between the scapulæ and is due to the jet produced by the stricture It may spill into diastole as demonstrated phonocardiographically by Wells Rappaport and Sprague (1949) It was heard high up in the typical situation in 85 per cent of the present series and in four cases in which aortic stricture was proved to be subphrenic (only one of them thought to be congenital) the murmur was only heard posteriorly in the lumbar region and anteriorly through the abdominal wall There is therefore strong evidence that the site of the posterior murmur at once distinguishes classical coarctation from the subphrenic variety According to both Abbott (1928) and Reifenstein *et al* (1947) there is complete occlusion of the aorta at the site of coarctation in about one quarter of all cases

come to necropsy It is not unlikely therefore that the 15 per cent of my series that did not have the murmur had complete occlusion It is admitted that large collateral vessels may sometimes cause a murmur, for digital compression of such a vessel may abolish it but this is exceptional and as a rule the murmur cannot be influenced by digital compression of any of the palpable collateral arteries That a coarctation jet may cause a murmur (and thrill) has been verified at operation

Electrocardiogram

In the present series the electrocardiogram was strictly normal in 46 per cent and showed slight left ventricular preponderance, as judged by the voltage of QRS in 23 per cent Marked left ventricular preponderance with inverted T waves in leads V_5 and V_6 occurred in 20 per cent and three quarters of these cases had well developed aortic valve disease usually stenosis Thus in uncomplicated coarctation only 5 per cent of cases showed electrocardiographic evidence of serious left ventricular strain

Right bundle branch block occurred in 11 per cent only a quarter of this small group had a patent ductus the other cases being straightforward Ziegler (1954) suggested that right bundle branch block might represent a residual change from strong right ventricular preponderance in utero when the fœtal ductus joined the aorta above the stricture

X ray appearances

There are three virtually diagnostic X ray signs of coarctation of the aorta, elongation of the aortic knuckle due to dilatation of the left subclavian artery (64 per cent) post stenotic dilatation of a short segment of the descending aorta which can be seen clearly in the postero anterior view (61 per cent) and notching of the inferior margin of the ribs (51 per cent) The figures given are from my own series

Dilatation of the left subclavian artery also obliterates the supraaortic triangle in the second oblique position (Evans 1952) Even when not distinguished clearly in the anterior view it seems to change the outline of the aortic knob so that the latter rarely looks normal

Post stenotic dilatation of the proximal end of the descending aorta immediately below the stricture was described by Bramwell (1947) as a double aortic knuckle (fig 8 11) It is a most important sign for it shows the presence and site of the stricture itself

Notching of the inferior margins of the ribs (fig 8 12) known as Dock's sign, is due to pressure erosion from dilated intercostal arteries (Railsbach and Dock 1929 Dock 1948) In my series it was seen in only one fifth of children under 12 years of age the youngest with notching was six Its higher incidence in past literature (about 80 per cent) may be due to the fact that coarctation was frequently overlooked in children and that notching of the ribs *per se* was perhaps the chief means of detecting it

Enlargement of the left ventricle was relatively slight or radiologically absent in 85 per cent of the cases Considerable enlargement was present

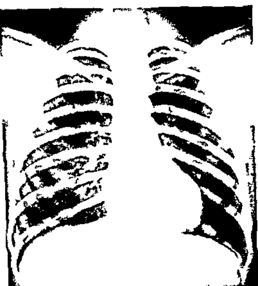


Fig 8 11—Post stenotic dilatation of the top of the dorsal aorta in a case of coarctation

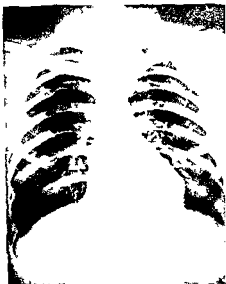


Fig 8 12—Rib notching (Dock's sign) in coarctation of the aorta



Fig 8 13—Mild coarctation of the aorta demonstrated by means of angiocardiography there is post stenotic dilatation of the proximal segment of the dorsal aorta and overlapping of proximal and distal segments owing to the plane in which the picture has been taken



Fig 8 14—The abrupt type of coarctation of the aorta demonstrated by selective angiocardiography diagnol having been injected directly into the pulmonary artery through a wide bore catheter

in 15 per cent but nearly all of these cases had serious aortic valve disease or were otherwise complicated

Entirely normal X ray appearances were seen in only 5 per cent of cases Aortic aneurysm usually mycotic and very close to the stricture was seen in two instances

The constriction itself (figs 8 13–8 16) may be demonstrated clearly by means of angiocardiography (Grishman Steinberg and Sussman 1941) or retrograde aortography (Broden Hanson and Karnell 1948)



Fig 8 15—Angiocardiogram demonstrating the hooked type of coarctation



Fig 8 16—Angiocardiogram in a case of coarctation of the aorta with complete occlusion showing marked dilatation and tortuosity of collateral channels

ASSOCIATED ANOMALIES

Bicuspid aortic valve occurred in 23 5 per cent of 200 autopsied cases reviewed by Abbott (1928) and in 42 3 per cent of 104 autopsied cases reviewed by Reifenstein Levine and Gross (1947) It is the usual cause of the aortic diastolic murmur that has been heard so frequently—in 20 per cent of 96 cases reported by Christensen and Hines (1948) and in 10 per cent of the author s series It was recorded phonocardiographically by Wills Rappaport and Sprague (1949) in 5 out of 15 cases of coarctation Aortic incompetence is rarely severe however unless bacterial endocarditis supervenes

Significant aortic stenosis presumably congenital occurred in 7 5 per cent of the author s series and calcific aortic stenosis was reported at necropsy in 11 per cent of the fatal cases collected from the literature by Reifenstein *et al* (1947) The presence of calcium however does not invalidate a congenital etiology (Campbell and Kauntze 1953) The stenosed valve is usually bicuspid (Smith and Matthews 1955) It is by no means easy to be sure whether aortic stenosis is present or not in cases of coarctation with

a basal systolic thrill and large left ventricle A convincing anacrotic pulse is exceptional the blood pressure is still raised and the aortic second sound may be loud An aortic systolic thrill without any other evidence of stenosis was appreciated in only three per cent of the series Two other cases thought to have some degree of aortic stenosis on account of considerable left ventricular enlargement and strong-left-ventricular preponderance electrocardiographically in addition to the thrill did not have a pressure gradient across the aortic valve at operation although in one of them the central aortic tracing looked stenotic in form Although the significance of a systolic thrill over the root of the aorta in cases of coarctation must remain in doubt the fact remains that judged on other grounds particularly on the size of the left ventricle and electrocardiographic evidence of left ventricular strain 75 to 85 per cent of such cases have aortic stenosis

The lesion is important because it increases the risk of surgical repair and because such repair may be valueless unless aortic valvotomy is also undertaken

Patent ductus arteriosus with most of the usual clinical features occurred in 7 per cent of my series The shunt was always from left to right whether the ductus joined the aorta above or below the stricture Rib erosion and a demonstrable collateral circulation were evident in only one instance their absence in the presence of patent ductus being noted by Bramwell (1947) in his three cases

Four remarkably illustrative cases were published by Edwards *et al* (1949) judged by the clinical features the microscopical appearances of the small pulmonary vessels and the relative sizes of the two ventricles at necropsy there was pulmonary hypertension with reversed shunt in two of them and a direct aorto pulmonary shunt in the other two the ductus joined the aorta above the coarctation in one of those with reversed shunt and in one with direct shunt and it joined below the coarctation in one each of these two functionally different types also

Patent ductus presents no special problem when complicating coarctation of the aorta in children or adults It should be ligated or divided at the same time as the stricture is repaired provided the shunt is from aorta to pulmonary artery if the shunt is reversed both the ductus and the coarctation should be left alone

Ventricular septal defect complicating coarctation of the aorta occurred in 2 per cent of this series and presents a rather similar physiological picture the raised pressure in the left ventricle tending to increase the left to right shunt

In a case investigated by the author and subsequently proved at necropsy the mean pulmonary arterial pressure was 95 mm. Hg whilst that in the right ventricle was 55 mm. Hg Samples from the pulmonary artery were 86 per cent saturated with oxygen from the middle of the right ventricle 70 per cent and from the right atrium and superior vena cava 60 per cent Clinically coarctation of the aorta was recognised by the presence of high blood pressure in the carotid



Fig 8 17—Coarctation of the aorta associated with patent interventricular septum proved at necropsy

and subclavian arteries (160 100 mm Hg in a boy of six) with an immeasurable pressure in the legs but there was little evidence of a collateral circulation The pulmonary arteries were grossly engorged radiologically (fig 8 17) there was a pulmonary diastolic murmur at the base and a mitral diastolic murmur with triple rhythm at the apex Despite the absence of a machinery murmur patent ductus arteriosus was believed to be responsible for the shunt and seemed to be confirmed by the catheter findings the raised oxygen content of the right ventricular sample being attributed to pulmonary incompetence At necropsy coarctation of the aorta of the adult type was associated with a large defect of the membranous interventricular septum The aortic cusps were normal the aortic ring admitted only the little finger and the ascending aorta was small The defect in the septum admitted the middle finger whilst the pulmonary ring admitted both middle and fore fingers A very small patent ductus joined the aorta below the isthmus Although the huge pulmonary artery did not sit astride the septal defect there could be no doubt that the major portion of the left ventricular contents was expelled into that vessel The mitral diastolic murmur was clearly functional for there was no sign of mitral stenosis Both ventricles were greatly enlarged the left retaining its natural dominance

Fibroelastosis (q v) appears to be the chief cause of heart failure and death in infants with coarctation of the aorta and usually makes surgical repair at that age pointless (Bonham Carter 1955) *It seems to be rare in* the large number of cases that survive infancy Whether a minor degree of fibroelastosis is responsible for an unusual degree of left ventricular

enlargement in children or for any of the aortic or mitral anomalies sometimes associated with coarctation is unknown

Variations in one or other subclavian artery rarely both occur in about 5 per cent of cases (King 1937) and may be due to its anomalous or stenotic origin (East 1932 Love and Holms 1939). Presubclavian coarctation is a rare cause of a small pulse in the left arm

COMPLICATIONS

Since practically all the important complications of coarctation of the aorta used to be fatal their relative frequencies are known from previous necropsy studies. The figures from two carefully documented series in the literature those by Abbott (1928) and by Reifenstein Levine and Gross (1947) are tabulated below

FREQUENCY OF COMPLICATIONS

CAUSE OF DEATH	ABBOTT (per cent)	REIFENSTEIN *et al* (per cent)	AVERAGE AGE (years)
Aortic rupture (or dissection)	20	23	25
Bacterial endocarditis (or endarteritis)	16	2	2)
Cerebral vascular accident	12 5	11	28
Congestive heart failure	29	18	39
Incidental	22 5	26	47

Aortic rupture is through the ascending aorta in 80 per cent of the cases and just distal to the coarctation in the remainder. The ascending aorta is thin walled and rupture usually means dissection into the pericardium (Reifenstein *et al* 1947)

Bacterial endocarditis infecting a bicuspid aortic valve is three times more common than bacterial endarteritis involving the aorta immediately adjacent to the coarctation usually just below it (Reifenstein *et al* 1947)

Saccular aneurysm of the descending aorta in the immediate neighbourhood of the stricture usually just below it is seen in about 3 per cent of cases (Abbott 1928 Gross 1953) and is nearly always secondary to bacterial endarteritis. There were two instances in the present series of 90 cases both of which were due to previous bacterial endarteritis. Calcification in the wall of the aneurysm is the rule and occurred in each of the two mentioned. One of them had the coarctation and the aneurysm excised and successfully replaced with a graft by Sir Russell Brock

Cerebral vascular accidents usually subarachnoid hemorrhage may be due to rupture of a berry aneurysm or of a vessel weakened by defective or

degenerative elastic tissue (Glynn 1940) Similar defects may be found in other vessels including the aorta (Davies and Fisher 1943) Hypertension presumably encourages the disaster

Heart failure is rare in uncomplicated cases under 40 years of age but takes an increasing toll as age advances even then some new complication may be responsible as in two of three cases that were observed over a period of 25 to 30 years when the development of heart block precipitated the breakdown (Newman 1948) As previously stated heart failure in infancy is usually due to associated fibroelastosis and in children or relatively young adults to aortic stenosis or incompetence bacterial endocarditis other congenital anomalies such as patent ductus and ventricular septal defect or coincidental rheumatic heart disease

Mitral valve disease may complicate coarctation of the aorta but probably not more often than would be expected from its known frequency of 2 per cent in the general population Unquestionable rheumatic mitral stenosis occurred in only two of the series reported here and in one of them Sir Russell Brock undertook mitral valvotomy at the same time as he successfully repaired the coarctation Relatively mild organic mitral incompetence may be aggravated by the hypertension associated with coarctation but this was only witnessed in one instance Amongst the children there was only one convincing case of rheumatic valvulitis in which a soft mitral diastolic murmur was heard for the first time after an attack of rheumatic fever Congenital mitral stenosis was not observed in this particular series but is a real although rare association

Pregnancy in cases of coarctation deserves a note The raised blood pressure may be discovered for the first time in an ante natal clinic and this is one of the standard ways in which the presence of coarctation comes to be recognised Of 96 instances collected from the literature by Rosenthal (1955) including 5 of his own 11 died during pregnancy chiefly from aortic rupture just before or during labour

PROGNOSIS AND TREATMENT

Although many patients live well into middle life without serious handicap some even to the eighth decade the majority succumb between the ages of 20 and 40 to one of the complications mentioned above (Abbott 1928) The average age of death is 35 (Reifenstein Levine and Gross 1947) Surgical repair (Crafoord and Nylin 1945 Crafoord 1948) should therefore be offered The physiological results of such an operation are usually good the blood pressure falls symptoms disappear the heart becomes smaller and it may be assumed that the risks of intracranial hæmorrhage aortic rupture and late heart failure are diminished Bacterial endocarditis on bicuspid aortic valves should not be prevented

The constriction is excised and the two ends joined together by direct suture or by means of an aortic homograft (Gross 1951) A patent ductus

may be ligated or a post stenotic mycotic aneurysm removed at the same time The mortality rate attending the resection has fallen from 16 per cent in 1949 (Shapiro) to under 5 per cent A series of papers by Gross (1949 1950 1953) illustrates this very well by 1953 he had operated on 270 cases in the first hundred of these (reported in 1950) there were eleven deaths in the last hundred only two Over the last five years our total surgical mortality rate at the Brompton hospital has been 8 per cent According to Gross (1953) the optimum time for the operation is between the ages of 10 and 20 years but 11 per cent of his cases were between 30 and 40 years old and the blood pressure may fall to normal even at this age Grafts become endothelialised but remain inert They seem capable of withstanding the blood pressure indefinitely

Selection of cases for surgery

Now that the operative mortality rate is under 5 per cent it is probably right to advise all patients with uncomplicated coarctation of the aorta to have it repaired between the ages of 7 and 30, the earlier the better An exception should be made if the stricture is trivial judged by a normal or near normal blood pressure good femoral pulsation without clinically detectable delay and no collateral circulation clinically or radiologically The diagnosis in these rare cases is made on the presence of a coarctation murmur posteriorly and post stenotic dilatation of the aorta radiologically it may be confirmed by means of angiocardiography

The effect of complications on the question of surgical treatment has already been discussed

RIGHT SIDED AORTA

As an isolated anomaly a right sided aortic arch joining a right dorsal aorta is rare and is discovered radiologically by chance (fig 4 31) Its radiological features (Bedford and Parkinson 1936) have already been described in Chapter IV Clinically it is of no significance

It may be important however when associated with other congenital anomalies because its presence may help their identification For example a right sided aorta occurs in some 20 per cent of cases of Fallot s tatralogy but not in pulmonary stenosis with normal aortic root again it may occur in Eisenmenger s complex proper but not in pulmonary hypertension with reversed shunt through a patent ductus or atrial septal defect

AORTIC RINGS

During the development of the aortic system certain anomalies may arise which may compress the œsophagus or trachea and cause dysphagia or distressing attacks of wheezing and choking in infancy Broncho pneumonia is a common complication and not infrequently fatal If the infant survives symptoms usually disappear as the vessels lengthen (Apley,

1949) but may return again with middle age owing to the development of arteriosclerosis (Sprague *et al* 1933) The chief anomalies responsible for this clinical syndrome are double aortic arch aberrant right subclavian artery and a ligamentum arteriosum joining a right aortic arch to the left pulmonary artery (Gross and Neuhauser 1951) The vascular arrangements are varied (Edwards 1948) but the three most common varieties may be described here

In *double aortic arch* the primitive fourth right arch which normally involutes distal to the innominate artery persists and joins the primitive *left* dorsal aorta Beyond the origins of the right subclavian and right common carotid arteries anteriorly the anomalous vessel courses posteriorly behind the trachea and œsophagus and links up with the normal anterior arch below the origin of the left subclavian artery where they join to become a left dorsal aorta The effect is to encircle the trachea and œsophagus

A *right sided aortic arch crossing behind the œsophagus* to join a left dorsal aorta may constrict the œsophagus and trachea by being pulled forward by a patent ductus or ligamentum arteriosum connecting it to the left pulmonary artery (Neuhauser 1949) It should be understood that an ordinary right sided aortic arch joins the *right* dorsal aorta the left dorsal root involuting so that the completed aorta courses down the right side of the thorax and causes no trouble

An *aberrant right subclavian artery* arises from the aorta distal to the left subclavian artery and passes across to the right and upwards behind the œsophagus, which it indents obliquely The filling defect of the barium filled œsophagus can be seen radiologically (Brean and Neuhauser 1947) *Lifelong dysphagia has been caused by this anomaly (Bayford 1789)*

All three anomalies may be modified surgically in such a way as to relieve the pressure on the trachea and œsophagus In double aortic arch the anterior channel can be divided between the left common carotid and left subclavian arteries a patent ductus or ligamentum arteriosum completing a vascular ring can be divided and an aberrant subclavian artery can be divided collateral pathways ensuring an adequate blood supply to the limb (Gross and Neuhauser 1951)

The whole rather complicated subject has been well reviewed by Brown (1950)

AORTIC HYPOPLASIA

Hypoplasia of the aorta is a common manifestation of Marfan's syndrome (q v) as pointed out by Baer Taussig and Oppenheimer (1942) Only the ascending aorta is usually involved especially at its root within the pericardium Pathologically it presents initially with features indistinguishable from cystic medial necrosis and later with degeneration and disruption of the elastic lamellæ disorganised masses of hypertrophic and hyperplasic smooth muscle, and numerous dilated vascular channels

penetrating the media from the adventitia (McKusick 1955) At first it is clinically unrecognisable unless the ascending aorta looks peculiarly small Sooner or later however dilatation of the aortic ring may lead to free aortic incompetence, the ascending aorta may become obviously dilated or the aorta may rupture or dissect without warning usually into the pericardial sac

Coarctation of the aorta is rarely associated with arachnodactyly but the pathological appearances of the ascending aorta in cases of aortic rupture or dissection secondary to coarctation are similar to those described above

Occasionally hypoplasia of the aorta is seen without any such associations and in rare instances hypoplasia and dilatation of the pulmonary artery accompany it (fig 8 18) The case illustrated was in a man of 33 with no symptoms and no abnormal physical signs cardiac catheterisation also revealed nothing abnormal

In these days of mass radiography difficulty may be experienced in trying to interpret the significance of an unusually prominent aorta as an isolated finding in a young individual The attitude advised is to take a serious view of any such anomaly if there is any trace of Marfan's syndrome in the family or if the apparent dilatation ceases abruptly at the origin of the innominate artery if neither condition applies the peculiarity may be better disregarded for the time being and treated as a normal variation

CONGENITAL AORTIC INCOMPETENCE

Aortic incompetence may be due to a bicuspid or quadricuspid aortic valve (*vide infra*) especially under the stress of hypertension whether acquired or due to associated coarctation of the aorta anomalous aortic valve cusps however may leak without any complication sometimes quite freely

The second important cause of congenital aortic incompetence is dilatation of the root of the ascending aorta as seen characteristically in Marfan's syndrome (q v) The leak in these cases is usually considerable and may be already well advanced at a time when the radiologically visible part of the ascending aorta still looks normal The prognosis in such cases is poor the risks being aortic rupture or dissection and heart failure

A third and rare cause of congenital aortic incompetence is ventricular septal defect (q v)

BICUSPID AORTIC VALVE

Abbott (1932) estimated the incidence of bicuspid aortic valve at 1 3 to 1 4 per cent Owing to the frequency of superimposed infection or sclerosis it is often difficult to be sure microscopically whether a disorganised valve is congenitally bicuspid or not but Lewis and Grant (1923) put its scopic recognition on a firm basis

1949) but may return again with middle age owing to the development of arteriosclerosis (Sprague *et al* 1933) The chief anomalies responsible for this clinical syndrome are double aortic arch aberrant right subclavian artery, and a ligamentum arteriosum joining a right aortic arch to the left pulmonary artery (Gross and Neuhauser 1951) The vascular arrangements are varied (Edwards 1948) but the three most common varieties may be described here

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At the time of Abbott s review 46 per cent of 147 proved cases and 21 per cent of 316 proved or probable cases of bicuspid aortic valve had coarctation of the aorta Conversely she calculated that 28 5 per cent of cases of coarctation had a bicuspid aortic valve Its significance in this condition has already been described

Apart from its association with coarctation bicuspid aortic valve is clinically important for three main reasons (1) it may leak spontaneously or as a result of acquired hypertension an insidious sclerosing process increasing this tendency (2) about one quarter of all cases become infected sooner or later (3) an associated weakness of the sinuses of Valsalva may lead to aneurysmal dilatation or rupture

AORTIC ATRESIA

Clinically this is unimportant since it is rarely compatible with more than a few days of life (Roberts 1936) it is also very uncommon (Brown 1950) Pulmonary hypertension with reversed shunt through a patent ductus allows venous blood to be transported to the systemic circulation Oxygenated blood can only escape from the lungs via broncho pulmonary anastomotic venous channels unless there is an atrial septal defect or anomalous pulmonary venous drainage Even with a large atrial septal defect the situation is wholly unsatisfactory for if a proper systemic output is to be maintained the pulmonary vascular resistance must be very high and this must prevent an adequate pulmonary blood flow According to Horley (1955) all reported cases have had fibroelastosis of the left ventricle unless the interventricular septum has been patent He suggests that both the complete fusion of the aortic cusps and the fibroelastosis may be due to anoxia resulting from the temporary formation of a complete im penetrable interatrial septum during some period of its development

AORTIC STENOSIS

Pathology

Congenital aortic stenosis may be valvular due to fusion of the cusps or subvalvular due to defective absorption of the primitive bulbus cordis, in the latter type a perforated membrane lies proximal to the valve (Keith 1924) Although in Abbott s necropsy series of 1 000 cases of congenital heart disease aortic valve stenosis was present in 11 and subaortic stenosis in 12 (Abbott 1931 and 1951) it is now generally believed that the great majority of cases are valvular All degrees of severity are encountered and it is probable that some of the relatively mild cases end up with calcific stenosis when they may be mistaken for rheumatic strictures (Campbell and Kauntz 1953) Even at necropsy it may be very difficult if not impos sible to make certain of the etiology when infective or sclerosing processes have grossly distorted the whole structure of the valve It is not possible clinically to distinguish the two types of congenital aortic stenosis

Incidence

Aortic stenosis accounted for 3 per cent of the 900 cases of congenital heart disease in this series There were three males to one female as in Campbell s series A congenital etiology was accepted if a loud aortic systolic murmur was first heard in infancy if any other congenital anomaly was present if there was a strongly suggestive family history such as that described by Davies (1952) or if an obviously tight stricture was found in childhood in the absence of a history of rheumatism or chorea

Clinical features

Although the clinical features of congenital aortic stenosis are more or less similar to those of acquired rheumatic stenosis (q v) there are minor points of difference that deserve emphasis

Of the 30 patients in the author s series only five of whom were over 18 years old symptoms were absent in 18 slight in two and moderate in five None had frank left ventricular failure Only one had angina pectoris and only two had syncopal attacks on effort For the most part therefore aortic stenosis is well tolerated in those that survive infancy infant mortality however is high the average age of death in Abbott s series for example being 3 75 years and this must account for the rarity of severe cases in later childhood and adolescence

Of the well known physical signs of aortic stenosis (q v) the peripheral pulse was normal in 15 small but not otherwise characteristic in 12 and detectably anacrotic in only three The left ventricle was a little heaving clinically in two thirds (but rarely displaced much to the left) normal or a little bulky radiologically (but not dilated) in 86 per cent and hypertrophied electrocardiographically in two thirds (considerably so with inverted T waves in leads V_5 and V_6 in a quarter) A loud aortic systolic ejection murmur usually heard as well at the apex as at the base and always accompanied by a well marked thrill was heard in all and since our attention was drawn to it by Leatham (1954) an aortic ejection click has also been heard in all but one instance The second heart sound was split normally in half the cases A falling before P it was clinically single in a third however due to delay in the aortic component and the split was reversed in two instances When single the second sound could usually be well heard over the carotid and over the left ventricle at the apex beat as well as at the base from which the presence of the aortic element was inferred An aortic diastolic murmur was heard in only 10 per cent which contrasts rather strongly with the 45 per cent incidence of associated aortic incompetence in the series reported by Campbell and Kauntz (1953) but this may be a matter of selection for we were at first disinclined to accept a diagnosis of congenital aortic stenosis in the presence of obvious incompetence A soft mitral diastolic murmur indistinguishable from that heard in many cases of coarctation of the aorta was detected in one sixth of this small series

The electrocardiogram provided the best evidence of the degree of left ventricular hypertrophy and has already been referred to

The X ray appearances were very similar to those described by Campbell and Kauntz (1953) The ascending aorta is usually a little prominent and curved out to the right but the aortic knuckle is normal or inconspicuous The left ventricle looks dense and hypertrophied rather than dilated so that the cardiothoracic ratio is not much increased

Cardiac catheterisation in six relatively mild cases revealed normal pulmonary artery pressures normal arteriovenous oxygen differences (average 32 ml per litre) and of course normal cardiac outputs

Prognosis

Severe cases usually die in infancy The majority of those seen in childhood are mild or relatively so and have a good prognosis Precise figures are difficult to arrive at in view of uncertainty concerning etiology in old calcific cases of aortic stenosis A minority in which the stenosis is more severe may die suddenly when young especially those with a history of angina pectoris or syncope on effort (Marquis and Logan 1955)

TREATMENT

Aortic valvotomy should be advised when serious symptoms begin to develop in severe cases

MITRAL STENOSIS

Congenital mitral stenosis is exceptionally rare being found in only six of Abbott s 1 000 cases Three examples are included in my own series of 900 clinical cases, one of them confirmed at operation Out of 43 collected from the literature by Ferencz Johnson and Wigleworth in 1948 (to which they themselves contributed nine) only eight were isolated by far the most common association was fibroelastosis (25) next came patent ductus (17) then aortic valvular stenosis (12) coarctation of the aorta (7) and ventricular septal defect (2) The great majority died in infancy

The clinical features appear to be similar to those of rheumatic mitral stenosis but are usually modified by the associated lesion In those who survive infancy the commonest associated lesions are patent ductus and coarctation of the aorta

Mitral valvotomy is advised if the symptoms warrant it although it may be awkward technically owing to difficulty in recognising exactly where the commissures should be D Abreu undertook the operation in two cases one of which had a patent ductus (Bower *et al* 1953) and Sir Russell Brock operated on one for me ligating a patent ductus at the same time

The increased pulmonary blood flow from the patent ductus might be expected to cause death from pulmonary œdema at an early age in these cases but in the patient mentioned a girl of 19 the pulmonary vascular resistance was high and cyanosis from shunt reversal began when she was only 18 months old and may

well have saved her life Cyanosis on effort increased a little over the years and was sufficiently differential to cause no clubbing of the fingers but at least moderate clubbing of the toes the hæmoglobin was 104 per cent there was of course no Gibson murmur the physical signs being those of mitral stenosis with moderate pulmonary hypertension and X rays showing a combination of pulmonary venous congestion and slight plethora Cardiac catheterisation (when she was 17 years old) revealed an indirect left atrial pressure of 18 mm Hg above the sternal angle a pulmonary artery pressure of 96/58 (rising to 130/90 on effort) a simultaneous right brachial pressure of 120/60 and bidirectional shunt the pulmonary artery sample being 74 per cent saturated the right ventricular sample 65 per cent and the right brachial 87 per cent Unfortunately no femoral sample could be obtained at the time but from our experience of reversed shunts in patent ductus (confirmed by means of angiocardiography in this case) the femoral sample could hardly have been above 80 per cent saturated The pulmonary blood flow worked out at 6 litres per minute and the pulmonary vascular resistance at 10 units It was argued that although shunt reversal was taking place the pulmonary blood flow was still above normal the pulmonary resistance was only borderline between high and extreme and that if the left atrial pressure were lowered the left to right shunt would increase It was decided therefore to advise ligating the duct as well as mitral valvotomy At operation the mitral orifice measured 1 25×0 75 cm and the duct 1 5 cm long and 1 5 cm wide both much as predicted

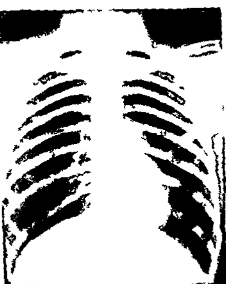
A year later she was looking and feeling well there was no cyanosis and no evidence of right ventricular embarrassment while her effort tolerance had increased considerably There were still well marked signs of mitral stenosis however for a complete valvotomy had not been achieved owing to the technical difficulty mentioned earlier

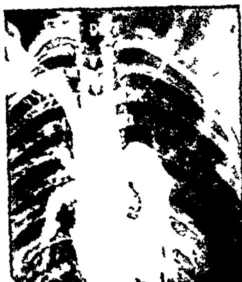
COR TRIATRIATUM

A physiological situation very similar to that produced by congenital mitral stenosis may be caused by the anomalous development of a transverse septum which separates that part of the left atrium joined by the pulmonary veins from the rest of the chamber In the case reported by Barnes and Finlay (1952) the anomalous septum was perforated by a small hole measuring only 2 mm in diameter through which the whole cardiac output had to pass There was intense pulmonary venous congestion but no evidence of mitral stenosis Pedersen and Therkelsen (1954) described a similar case in which cardiac catheterisation revealed typical evidence of mitral stenosis at operation the mitral valve was normal and the anomalous septum was overlooked

IDIOPATHIC DILATATION OF THE PULMONARY ARTERY

Mass radiography brings an increasing number of cases for cardiological review on account of real or apparent dilatation of the pulmonary artery as an isolated abnormality Quite a number of such cases can be dismissed





(a) Anterior view (b) Angiocardiogram

Fig 8 19—Apparent dilatation of the pulmonary artery in a normal subject

immediately as variants of normal or as rotational effects (fig 8 19) In the example illustrated the left pulmonary artery is responsible for the left middle arc and the angiocardiogram prove that the pulmonary artery is not dilated (cf fig 8 16c) There remain however a small group of cases in which the pulmonary artery is undoubtedly dilated for no apparent reason (Laubry Routier and de Balsac 1941)

There are no symptoms and no abnormal physical signs in uncomplicated cases except a pulmonary ejection click which is common and a soft pulmonary systolic murmur which is perhaps less common The second heart sound is physiologically split and the pulmonary component of average intensity The electrocardiogram is normal Angiocardiography is the only reliable way of proving the existence of true dilatation (fig 8 16c)

Cardiac catheterisation whilst demonstrating essentially normal pressures and flows not infrequently reveals a slight systolic pressure gradient of 5 to 10 mm Hg across the pulmonary valve the right ventricular pressure however is not above normal The significance of this phenomenon which was recorded consistently in four out of eight such cases catheterised and which was noted by Cournand Baldwin and Himmelstein (1949) is not yet understood Trivial pulmonary valve stenosis is difficult to exclude and in some of the cases the tracings themselves are unsatisfactory and suggest an artefactual gradient

Functional pulmonary incompetence may complicate cases of idiopathic dilatation and despite the normal pressure in the pulmonary artery may be considerable in degree Conspicuous dilatation of the right ventri

results and the electrocardiogram may show prolonged right ventricular activation Secondary tricuspid incompetence and final overloading of the right ventricle may complete the breakdown Admittedly such cases are rare but they may serve to correct an impression that pulmonary in competence is always harmless in the absence of a high pulmonary vascular resistance

Idiopathic' dilatation of the pulmonary artery is occasionally due to the same abiotrophy that affects the ascending aorta in cases of Marfan s syndrome and in these rare cases has been known to rupture A good example of the double lesion is illustrated in fig 8 18

EBSTEIN S DISEASE

A rare anomaly of which there were ten examples in the present series all diagnosed during life is malformation and displacement of the tricuspid valve (Ebstein 1866) With greater precision in diagnosis an increasing number of live cases are coming to light Helpful reviews are those by Yater and Shapiro (1937) Engle *et al* (1950) Baker *et al* (1950) and Medd *et al* (1954)

Pathology

The anterior cusp always retains some attachment to the annulus fibrosus but the posterior loses its connection entirely and is attached to the walls of the right ventricle (Brown 1950) The cusps themselves are also grossly malformed and present a curious basket like arrangement that is difficult to describe The right ventricle and atrium are grossly dilated the infundibulum distal to the valve usually less so The foramen ovale is patent and functions in varying degree in about two thirds of the cases

Clinical features

Males and females are affected equally There were six males and four females in the present series

Ages vary greatly according to the severity of the lesion and range from early childhood to 80 The ages of my patients when first seen were 13 15 25 28 18 months 14, 4 5 22 and 53

Symptoms are remarkably mild in relation to the size of the heart shadow radiologically and have been overrated in the literature Cyanosed cases have gravitated to special clinics in the hope of obtaining relief by means of cardiac surgery and after an unsuccessful operation or otherwise have tended to find their way into the medical press Thus the general impression seems to be that Ebstein s disease is a cyanotic form of con genital heart disease yet of the ten new cases reported here only one presented as such although the patient herself denied it and only one of three other cases that I catheterised for my colleagues was centrally cyanosed clinically Many of these acyanotic cases are still being overlooked and continue to masquerade under a motley variety of diagnoses

Effort intolerance was negligible in four of my cases, slight (grade 1) in four and moderate (grade 2A) in the other two. None were in the least disabled except during attacks of paroxysmal tachycardia (*vide infra*). In the worse cases dyspnœa and fatigue limit physical activity.

Attacks of faintness accompanied by intense cyanosis are probably due to paroxysmal tachycardia but they are unusual. Baker *et al* (1950) found only two examples in some 25 clinical records in the literature. In a case that I observed intense cyanosis accompanied paroxysmal *nodal* tachycardia that caused giant venous cannon waves and obvious reversed inter atrial shunt (fig 6 33). With normal rhythm the venous pressure oscillated gently around sternal angle level (fig 8 22) and central cyanosis was only just apparent (denied by the patient).

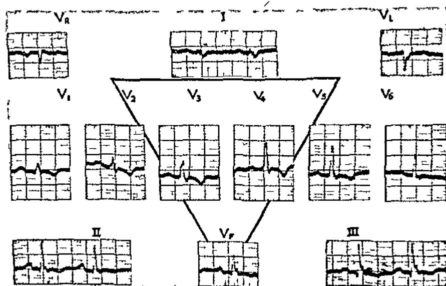


Fig 8 20—Electrocardiogram in Ebstein's disease showing a right bundle branch block pattern and rather low voltage

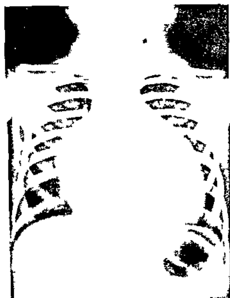
Physical signs

The physical signs are highly characteristic and together with the electrocardiogram and X ray appearances usually make the bedside diagnosis obvious.

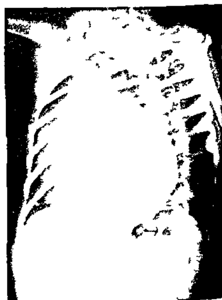
1. *Central cyanosis at rest clubbing and polycythæmia are usually absent.* Only one of my ten cases had these features. A second had doubtful cyanosis at rest but no clubbing. Three had a highly coloured moon facies peripheral cyanosis and no clubbing. The other five looked entirely normal. The majority of cases in the literature have been cyanosed from birth or have developed cyanosis in childhood or adolescence. The discrepancy is attributed to selected material.

2 The peripheral pulse is usually small and the blood pressure rather low, figures around 110/80 being typical

3 The venous pressure and pulse are of two kinds they are either inconspicuous, the pressure being around or below sternal angle level with *a*, *c* and *v* of rather low amplitude (fig 8 22) or they have the features of tricuspid incompetence (fig 8 23) giant *a* waves were *not* seen in any of my cases and a moderate *a* wave about 3 mm Hg above *v*, in only two instances The literature is not at its best in respect of the clinical venous pulse in Ebstein s disease but on the whole the findings seem to have been similar



(a) Anterior view



(b) Second oblique position

Fig 8 21—Typical skiagram in a case of Ebstein s disease showing gross dilatation of the right ventricle and atrium and clear lung fields

4 *The heart is quiet* On two occasions cases of pulmonary valve stenosis were referred as ? Ebstein s disease when there was a grade 3 right ventricular heave on another occasion a case of Ebstein s disease was referred as ? severe pulmonary valve stenosis when no cardiac impulse could be felt anywhere No convincing impulse could be felt over the right ventricle in any of these ten cases in one there was slight retraction A gentle localised left ventricular impulse was felt far out towards the axilla in at least three instances the point was not always recorded however—there was merely the statement that the heart felt unusually quiet

5 On auscultation most observers have commented on the frequency of gallop rhythm the extra sound being a right ventricular third heart sound Right atrial gallop is very unusual If the P R interval is prolonged right atrial contraction may accentuate the third heart sound

6 The moderately loud—presumably pansystolic—murmur that was heard over a wide area in about 80 per cent of cases in the literature accompanied by a thrill in three of my patients may be attributed to tricuspid incompetence

7 A very characteristic superficial diastolic scratch, giving the cadence of triple rhythm (disregarding the gallop sound) was heard in all but two cases in this series and has been mentioned in about half the recorded cases in which auscultatory details have been given It is usually heard best close to the sternum in the third left space, but in two of my cases it was louder *well to the right of the sternum* at the same level It sounds more like diastolic pericardial friction over the distended right atrium than a true intracardiac murmur occurring at a time when the right atrial pressure falls steeply maximal right atrial movement due to volumetric change provide a possible explanation but its exact mechanism awaits elucidation In two recent cases this diastolic murmur may well have been tricuspid for it was much accentuated during inspiration

Electrocardiogram

All observers have stressed the frequency of partial or complete *right bundle branch block*, which has been recorded in about 90 per cent of all cases There were no exceptions among the ten reported here The form of the complexes however is often a little bizarre as in the case illustrated (fig 8 20) and in eight out of the ten the voltage was low

Tall sharp P waves have been described in well nigh 80 per cent of published cases In the present series however P was inconspicuous (as in the illustration) in eight and prominent (3 or 4 mm high and 0 08 second wide) in two

The *P R interval* has been slightly prolonged (usually 0 24 sec) in a little over one third of cases In the present series it ranged between 0 14 and 0 2 second in eight out of the ten cases and was 0 24 second in the other two

X ray appearances

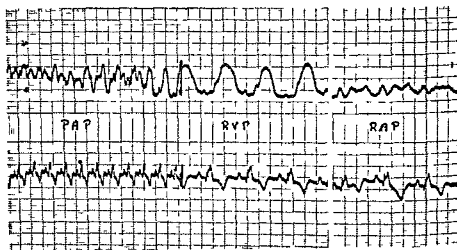
The radiological features of Ebstein s disease are as characteristic as the physical signs and the electrocardiogram The aorta is small and the lung fields clear and translucent The enormous relatively still heart shadow produces a sharp stencilled effect on the skiagram reminiscent of pericardial effusion (fig 8 21) the bulk of this shadow represents the distended right ventricle and atrium the former approaching the left lateral wall of the thorax the latter bulging far to the right

DIFFERENTIAL DIAGNOSIS

Faced with such a characteristic picture made up of so many striking and unusual features it is difficult to think of any other possible diagnosis If the history gives no indication of the duration of the condition peri-

cardial effusion might well be considered in acyanotic cases and was in fact the way one of my patients presented Like Ebstein's original case and five out of 28 reviewed by Baker *et al* (1950) this patient had pulmonary tuberculosis and the effusion had an all too ready explanation The Ebstein diastolic scratch lends superficial credence to such a diagnosis But the jugular venous pressure pulse the curious and unexpected gallop and the electrocardiogram should prevent error

In practice the commonest mistake has been confusion between Ebstein's disease and severe pulmonary valve stenosis with or without reversed interatrial shunt There is rarely much excuse for such an error for there are at least seven major points of difference (see pulmonary stenosis)



Paper speed 25 mm sec

Fig 8 22—Relatively normal intracardiac pressures in a case of Ebstein's disease

Cardiac catheterisation — C t

I have personally catheterised seven cases of Ebstein's disease but do not propose to catheterise another wittingly Three deaths due to catheterisation are known to me one being in the present series and paroxysmal tachycardia occurred in another of mine There need be no hesitation in using the catheter to disprove a case referred as Ebstein's disease if the real diagnosis is thought to be pulmonary valve stenosis on firm clinical grounds and the catheter can be used safely in the right atrium to check the possibility of pericardial effusion if there is any real doubt about the matter but in the great majority of cases the clinical diagnosis of Ebstein's disease is beyond question and should be left at that Of the ten cases in this series five were confirmed by means of catheterisation (two also at necropsy) and five have not yet been confirmed or catheterised but are still alive

The findings at catheterisation are as follows

1 All pressure pulses may be more or less normal but of rather low amplitude (fig 8 22) in the illustration the right atrial *c* wave is unduly prominent and has overcome the x descent This appears to be the rule

2 Right atrial and right ventricular pressure pulses are more or less indistinguishable and resemble right atrial tracings in gross tricuspid incompetence (fig 8 23)

According to Van Lingen (1952) it may be possible to locate the position of the tricuspid valve by demonstrating two ventricular chambers that portion proximal to the valve behaving like the right atrium that distal to the valve like a true ventricle

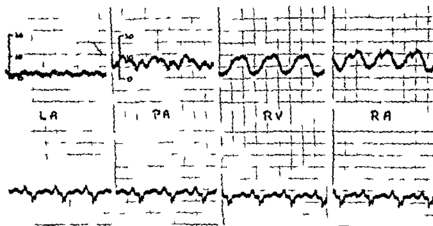


Fig 8 23—Tricuspid incompetence type of pressure tracings in a case of Ebstein's disease showing an almost identical systolic pressure in the pulmonary artery right ventricle and right atrium

3 The pulmonary artery pressure which was recorded in five of my seven cases is normal but low the systolic level being the same as that in the right ventricle distal to the tricuspid valve

4 The arterial oxygen saturation varies greatly according to the degree of reversed interatrial shunt In the horizontal position it is usually between 70 and 90 per cent saturated In my five successfully catheterised cases it was 87 83 78 72 and 90 per cent saturated But it would be interesting to know what it was in the vertical position One of these cases was clinically cyanosed at rest and she was the only one with an oxygen capacity above 190 ml per litre The pulmonary blood flow in four adults was 6 4 4 4 3 1 and 3 3 litres per minute—the fifth patient (aged 4) did not have her oxygen uptake measured

5 The pulmonary capillary venous pressure measured in two cases was normal (fig 8 23) proving that in these two cases any opening in the atrial septum could have been no more than a small foramen ovale

Prognosis and treatment

Life expectancy varies with the degree of cyanosis the average age of death in cases cyanosed from birth is 12 years whereas in acyanotic cases it is over 28 years (Baker *et al* 1950) Patients who are symptom free and wholly acyanotic have a good chance of surviving to middle age or beyond

No specific treatment is possible

ATRIAL SEPTAL DEFECT

Embryology Atrial septal defect refers to a relatively large non valvular opening in the atrial septum, through which blood may flow either way. Embryologically the atrial septum is formed in the first place by the sickle shaped septum primum which grows forwards from the dorsal wall of the common atrium, dividing it into two For a time communication exists between the two atria in front of the crescentic edge of the growing septum If development is arrested at this stage a septal defect results and is situated in the lower anterior part of the septum just below and usually including part of the fossa ovalis When growth proceeds normally this hole is obliterated and a new one the foramen ovale appears in the upper and dorsal part of the septum primum arrest at this stage results in a defect just above the site of the fossa ovalis With further normal development the foramen ovale comes to lie more anteriorly and is turned into a valve by the growth of the septum secundum on the right side of the septum primum and covering it at all points except over the area known as the fossa ovalis When the septum secundum develops fully and the septum primum degenerates completely the defect occurs at the site of the fossa ovalis

In *patent foramen ovale* the septa are fully developed, but imperfectly fused When pressure is applied to the right side of the fossa ovalis the septa are parted, blood penetrates between them and escapes into the left atrium through the patency in the upper part of the septum primum known as the foramen ovale proper In fœtal life the relatively high pressure in the right atrium keeps the valve open and causes blood to be shunted from right to left in order to avoid the pulmonary circulation At birth the pressure rises in the left atrium and forces the septum primum against the septum secundum thereby closing the valve In 80 per cent of all individuals fusion then takes place between the two septa and the foramen ovale is permanently closed In the remaining 20 per cent fusion fails and valvular patency continues It is then a potential cause of reversed interatrial shunt if for any reason the pressure in the right atrium comes to exceed that in the left This may happen in such conditions as pulmonary hypertension pulmonary stenosis and pulmonary embolism

A cardiac catheter may slip through a patent foramen ovale into the left atrium without difficulty and may enter the left ventricle (fig 8 24) or any of the pulmonary veins (fig 8 25) or the left atrial appendage (fig 8 26) The pressures and electrical potentials in these chambers may thus be



F c 8 24—Catheter n the left entricle via a patent foramen ovale



Fig 8 5—Catheter in a pulmonary vein via a patent foramen o ale

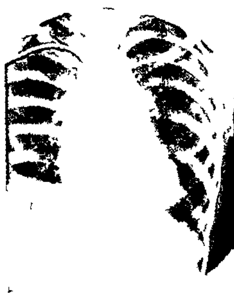


Fig 8 6—Catheter in l ft atrial appendag

obtained in favourable cases including otherwise normal hearts The mean left atrial pressure is about 4 mm Hg higher than the right Pulmonary venous samples have usually been around 96 per cent saturated with oxygen Uncomplicated patent foramen ovale is easily distinguished from atrial septal defect because of the absence of any appreciable inter atrial shunt as judged by samples from both atria and their respective venous systems

Hæmodynamics An atrial septal defect is usually 1 to 3 cm in diameter and carries a considerable shunt from left to right atrium, the right ventricle offering less resistance to filling than the left Oxygenated blood is thus added to the normal intake of the right ventricle the stroke output of which is correspondingly increased The shunt results in enlargement of the right atrium and ventricle dilatation of the pulmonary artery and pulmonary plethora Left atrial leakage deprives the left ventricle of its full intake, the left ventricular stroke output is diminished, the left ventricle and aorta hypoplastic and the pulse small Progressive right ventricular enlargement eventually leads to failure the pressure in the right atrium then rises and if it exceeds that in the left the shunt is reversed and cyanosis develops As a rule, however, the left atrial pressure also rises with heart failure and shunt reversal is prevented this may be due to a reversed Bernheim effect or to the pressure equalising influence of a stretched pericardium According to some authorities a high jugular venous pressure in A S D means left ventricular failure Cyanosis in A S D nearly always means an extreme pulmonary vascular resistance (see Eisenmenger s syndrome)

Incidence A S D accounted for 18 per cent of the author s series of 900 cases of congenital heart disease It shows a slight preference for females, the sex ratio being 3 2 in their favour The average age for the whole group was 23 years The number per cent in each decade was as follows

Age	1–10	11–20	21–30	31–40	41–50	51–60	61–70
No per cent	19	38	15	12 5	7	5	3 5

The oldest was 68 and the oldest on record 82 (Ellis Greaves and Hecht 1950)

Associated lesions Arachnodactyly high arched palate alone or obvious thoracic deformity alone (usually kyphoscoliosis or pigeon chest) occurred with equal frequency in one quarter of the cases Coincident mitral stenosis (Lutembacher 1916) whether congenital or acquired was recognised clinically in only two instances and discovered at operation in another It is difficult to understand the high incidence of Lutembacher s syndrome in past necropsies Bedford Papp and Parkinson (1941) for instance, put it at 25 per cent Current opinion has swung sharply away from this concept and finds support in modern figures concerning its frequency at post

mortem e g 6 per cent in the series reported by Nadas and Alimurung (1952)

CLINICAL FEATURES

Symptoms

The majority of uncomplicated cases of atrial septal defect have no symptoms This statement applied to 57 per cent of the author s series Effort intolerance was slight in 12 5 per cent moderate in 12 5 per cent considerable in 6 per cent and gross (total incapacity) in 12 per cent Of those with grade 3 or 4 effort intolerance 55 per cent were between the ages of 45 and 68 (average 55 5), of the remainder one third were infants

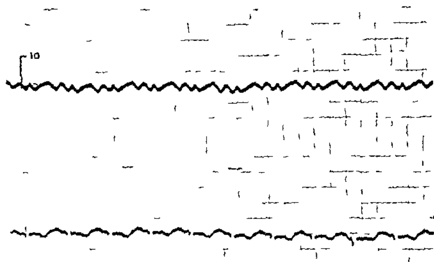


Fig 8 27—Normal right atrial pressure oscillating gently around zero in a case of A S D

one third ordinary severe cases in younger adults and one third owed much of their disability to other lesions such as emphysema polycystic kidney or mitral stenosis It follows that symptomless uncomplicated atrial septal defect in young adults is a relatively benign anomaly

Recurrent bronchitis or bronchopneumonia occurred in 10 per cent of all cases and was attributed to the tendency of already hyperæmic lungs to react excessively to minor respiratory infections

Hæmoptysis occurred in only 3 per cent and bronchial tuberculosis was responsible for the hæmorrhage in two of these cases

Physical signs

Patients with atrial septal defect are not infrequently under developed, frail or gracile in build and any of the associated congenital anomalies mentioned above may be present

The *peripheral pulse* is characteristically small The *jugular venous pressure* was strictly normal in 75 per cent of the series reported here (fig 8 27) slightly raised (about 3 cm above the sternal angle) with *a* and *v* more or less equal in amplitude in 17 per cent and high with a wave form suggesting tricuspid incompetence in 8 per cent The *right atrial pressure pulse* was recorded in 58 cases and confirmed these clinical observations Neither giant nor dominant *a* waves were seen in uncomplicated cases nor was *v* in any way remarkable except in those with tricuspid incompetence

The left ventricle is nearly always impalpable but a substantial systolic lift over the *hyperdynamic right ventricle* from the left sternal edge to the mid clavicular line or beyond is almost invariable *Pulmonary artery pulsation* in the second left space can be felt in 50 per cent of cases

There are several important auscultatory signs A *pulmonary ejection murmur* due to an increased pulmonary blood flow was heard in 80 per cent of the series and was accompanied by a thrill in one quarter of all cases When the thrill was very pronounced catheterisation or other physical signs usually demonstrated coincident pulmonary stenosis and such cases have been excluded from the group under consideration A pulmonary ejection click was heard occasionally but was unusual in the absence of a high pulmonary vascular resistance or slight pulmonary stenosis A *pulmonary diastolic murmur* due to functional pulmonary incompetence (Graham Steell murmur) was rare in the absence of pulmonary hyper tension but a soft *mid diastolic murmur*, usually in the third or fourth left space near the sternal edge or towards the apex of the right ventricle was heard in 30 per cent, This mid diastolic murmur which is accentuated during inspiration is attributed to turbulence set up at the defect itself or to a torrential tricuspid blood flow necropsies have disproved its mitral origin (except in Lutembacher's syndrome) The *second heart sound is widely split* and varies very little if at all with respiration The second or pulmonary element may be a little accentuated but is more often normal unless there is pulmonary hypertension The wide split was attributed by Barber Magidson and Wood (1950) either to right bundle branch block or to delayed emptying of the overfilled right ventricle perhaps to both Earlier closure of the pulmonary valve has been noted after successful repair of atrial septal defect without significant change in the electrocardio gram and right ventricular pressure curves timed against the electro cardiogram prove that there is no delay in the onset of right ventricular contraction (Leatham and Gray 1955) it follows that the wide split must be due to prolongation of right ventricular systole (or shortening of left ventricular systole) Failure of the split second heart sound to widen on inspiration was first noticed by Mr W W Dicks the senior cardiological technician at the London Hospital and was confirmed by Fowers (1952) and by Leatham and Gray (1955) we have assumed that the greatly distended right ventricle is unable to fill much more on inspiration, or that



Fig 8 28—Skiagram of a case of atr al septal def ct showing dilatation of the pulmonary art ry and its branches enlargement of the r ght ventricle and atrium and hypoplasia of the aorta



(a) Antero posterior view



(b) First obliqu pos tion sho ing d latat on th left atrium

Fig 8 29—Lutembacher s yndrome

the increased inspiratory flow from the systemic veins into the right atrium tends to inhibit the shunt proportionally



Fig 8 30 —Atrial septal defect in a child aged 10

Fluoroscopy in well developed cases (fig 8 28) reveals gross dilatation and conspicuous pulsation (hilar dance) of the pulmonary artery and its branches peripheral pulmonary plethora enlargement of the right atrium and ventricle and hypoplasia of the aorta and left ventricle (Bedford Papp and Parkinson 1941) In Lutembacher s syndrome (fig 8 29) the left atrium is also enlarged In less advanced cases however and especially in children the changes described may be much less noticeable (fig 8 30)

Electrocardiograms show a partial or complete right bundle branch block pattern in 95 per cent of cases (fig 8 31) (Barber Magidson and Wood (1950) The prolonged activation of the right ventricle is almost certainly due to dilatation of that chamber and not to any real interruption of the right bundle branch The secondary R wave in lead V_1 seldom exceeds 10 mm in height in uncomplicated cases and is usually well under this The P wave was normal under 2 mm in height in 90 per cent of the present series when it is tall and sharp associated pulmonary stenosis or a high pulmonary vascular resistance should be suspected A slightly prolonged P R interval (around 0 24 sec) was seen in 10 per cent Atrial fibrillation occurred in 10 per cent of the whole series and was closely related to age thus it was found in only one patient under 30 years old in 12 5 per cent of those between 30 and 50 in 50 per cent of those between 51 and 60 and in 80 per cent of those over 60 years

The diagnosis may be proved by obtaining samples of relatively oxygenated blood from the right atrium, right ventricle, and pulmonary artery by means of cardiac catheterisation when samples from the venæ cavæ show ordinary venous blood (Howarth McMichael and Sharpey Schafer 1947) In 86 cases investigated at the Institute of Cardiology samples obtained from the right atrium right ventricle and pulmonary artery differed little and ranged between 75 and 90 per cent saturated with oxygen caval samples being normal (55 to 75 per cent saturated) Samples from the left atrium left ventricle and femoral artery were normal (94 to

96 per cent saturated) in about half the cases and between 84 and 93 per cent saturated in the other half According to Swan Burchell and Wood (1954) slight shunt reversal can usually be demonstrated by means of dye concentration curves especially when the dye is injected into the inferior vena cava and they think this explains the slightly reduced arterial oxygen saturation not infrequently found But in 12 cases in the present series pulmonary venous samples* were obtained and proved to be similarly unsaturated in five of them suggesting that hurry through a widely dilated pulmonary vascular bed may also be responsible In uncomplicated atrial

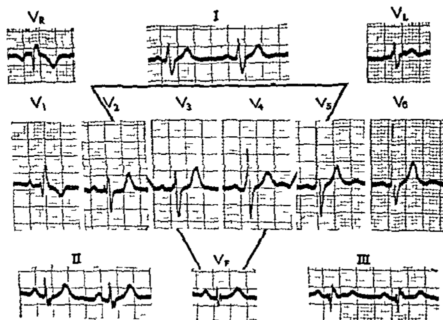


Fig 8 31—Electrocardiogram in a case of A S D showing a partial right bundle branch block pattern

septal defect the pulmonary blood flow is usually two to three times the systemic flow, i e about 10 to 15 litres per minute The systemic flow is commonly normal but may be reduced in severe cases

Pressure tracings from the two atria usually show little actual difference (fig 8 32) the potential gradient from left to right being masked by the flow It is assumed that the normal difference between left and right atrial pressure is due to greater resistance on the part of the left ventricle to

* In taking pulmonary venous samples the vessel must not be blocked by the catheter or the sample is bound to be 99 to 100 per cent saturated When a pulmonary vein is blocked the distal pressure rises sharply until it equals the pulmonary artery pressure and the tracing becomes arterial in form

diastolic filling i e to a higher diastolic tone in the left ventricle than in the right The greatest shunt flow may therefore occur during the period of rapid ventricular filling immediately after the opening of the tricuspid valve

The pulmonary artery pressure was normal or only slightly raised in 90 per cent of these cases and between 60/30 and 100/50 in 10 per cent excluding 15 cyanotic cases with an extreme pulmonary vascular resistance and reversed inter atrial shunt which are considered later in relation to Eisenmenger s syndrome It is clear that the normal long term reaction of the pulmonary arterial tree to the increased blood flow is vasodilatation This prevents any serious rise of pressure with flows up to 15 litres per

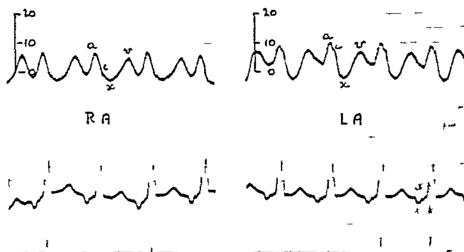


Fig 8 3.—Left and right atrial pressure tracings in a case of A S D showing a slightly higher pressure on the left side although the R A P is raised secondary to heart failure

minute (in an adult) with flows greater than this relatively harmless hyperkinetic pulmonary hypertension occurs without an increased pulmonary vascular resistance Over the years secondary vascular changes may increase the resistance a little but never seriously In 20 per cent of cases however the reaction is of an entirely different order in these the pulmonary vascular resistance is high being 5 to 9 units in the group discussed here (about half of the 20 per cent) and 10 to 20 units in those with reversed shunt This vasoconstrictive response seems to be determined at birth and is discussed more fully in connexion with Eisenmenger s syndrome

COMPLICATIONS

Pulmonary hypertension complicating atrial septal defect as described above may be recognised by exaggeration of the *a* wave of the jugular pulse a more sustained left parasternal heave a pulmonary ejection click

closer splitting of the second heart sound and obvious accentuation of the second or pulmonary—element free pulmonary incompetence greater dilatation of the pulmonary artery less pulmonary plethora with loss of peripheral arterial tapering, and the development of a tall sharp P wave in standard leads and of a higher voltage secondary R wave in lead V_1 of the electrocardiogram If the pressure in the right atrium comes to exceed that in the left central cyanosis develops and the peripheral pulmonary vascular shadows diminish

Tricuspid incompetence may result from gross dilatation of the right ventricle with or without pulmonary hypertension and is usual when there is *congestive failure* It is remarkable that the shunt does not usually reverse

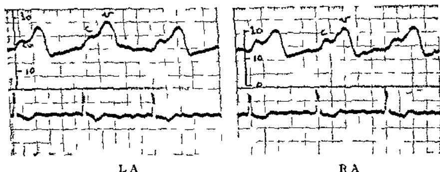


Fig 8 33—Pressure tracings from both atria in a case of A S D showing a slightly higher pressure on the left side despite marked tricuspid incompetence and a very high right atrial pressure

in such cases, despite right atrial pressures of 10 to 20 cm above the sternal angle That the left atrial pressure remains higher than the right even under these circum tances (fig 8 33) demands some special mechanism which increases the resistance to left ventricular filling Whether this is a reversed Bernheim effect a manifestation of left ventricular failure or due to the pressure equalising influence of a stretched pericardium is as yet uncertain

Pulmonary stenosis complicates atrial septal defect in about 10 to 15 per cent of cases. It may be very mild and may hardly alter the physical signs or the hæmodynamics but an impressive systolic thrill over the pulmonary artery is suggestive and a pulmonary artery pressure at least 10 mm Hg lower than that in the right ventricle is diagnostic

Severe pulmonary stenosis associated with atrial septal defect causes reversal of the interatrial shunt and a cyanotic form of congenital heart disease (q v)

Partial anomalous pulmonary venous drainage into the right atrium (q v) is not uncommon and increases the left to right shun

Bacterial endocarditis is very rare in uncomplicated cases of atrial septal defect (about 1 per cent) and its occurrence at once suggests associated pulmonary stenosis

PROGNOSIS

Of the 167 cases in this series five died naturally—three (aged 2 3 and 43) from congestive failure one from associated cor pulmonale and one from polycystic kidneys Five others died from attempted surgical repair all advanced cases and one (also in failure) died as the result of cardiac catheterisation The average age of these 11 patients (6 6 per cent of the series) was 21

According to McGinn and White (1933) and Roesler (1934) the average age of death in atrial septal defect is 35 to 36

On the whole however it is believed that the prognosis in uncomplicated cases with average shunts is good congestive failure being a late development and not to be expected before middle life This must influence selection of cases for surgical treatment

TREATMENT

Over the past few years a determined attempt has been made to find the best method of closing atrial septal defects Murray (1948) passed fascia lata sutures through the atrial septum in such a way as to occlude the defect but the method was too uncertain to be followed up Bailey (1953) closed many defects by suturing part of the wall of the distended right atrium to the interatrial septum making sure that free passage was preserved between the mouths of the venæ cavæ and the tricuspid orifice This technique has been used by many surgeons with considerable success but lacks the precision of direct suture Gross (1952 1953) showed that atrial septal defect could be closed by direct suture if a leak proof rubber well was first attached to the right atrial wall when the right atrium is opened blood rises in the well to a level which represents the central venous pressure and so maintains normal right ventricular filling and allows the surgeon to perform his task under water as it were Air embolism is avoided because the tricuspid valve is totally immersed The introduction of open heart surgery however made possible by hypothermia or crossed circulations has resulted in the modern method of closing the defect by simple suturing under direct vision (Lewis and Taufic 1953 Swan *et al* 1953) Subsequent physiological studies have proved that the defect remains closed (Blount *et al* 1954)

Eighteen of the present series were operated on six by Mr W C Cleland using Bailey s technique and twelve by Sir Russell Brock with the aid of hypothermia Although six of these patients died they were very advanced and the results in the survivors have been most gratifying

At the present time surgical repair should be recommended if the pulmonary blood flow is more than three times the systemic flow if the pulmonary vascular resistance is between 6 and 10 units or if there is obvious tricuspid incompetence or congestive heart failure Until the mortality rate is under 5 per cent uncomplicated cases with good effort

tolerance and 2 to 1 shunts should certainly be left alone With bidirectional shunt it is reasonable to advise repair *as long as the pulmonary blood flow is still increased* even though the pulmonary vascular resistance is above 10 units (800 dynes sec /cm^5) for the resistance may be expected to fall if the flow can be diminished but it is not reasonable to advise repair when an extreme resistance has resulted in a normal or reduced pulmonary blood flow and reversed shunt

PERSISTENT COMMON ATRIOVENTRICULAR CANAL

A common atrioventricular opening with deformed mitral and tricuspid valves is always associated with a persistent ostium primum (A S D) usually with a ventricular septal defect and often with mongolism

Of 55 cases reviewed by Rogers and Edwards (1948) over half died within the first year of life and only five survived to the age of 30

Clinically these cases usually present with all the features of an exceptionally large atrial septal defect complicated by mitral (as well as tricuspid) incompetence an appreciable number however have the Eisenmenger reaction and reverse the shunt

PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE

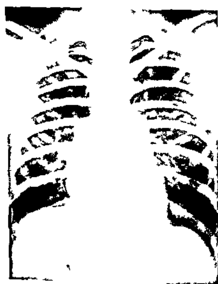


Fig 8 34—Skiagram showing an anomalous pulmonary vein joining the right atrium

One or more pulmonary veins may drain directly into the azygos superior vena cava right atrium or inferior vena cava According to Brody (1942) anomalous pulmonary veins are twice as frequent in the right lung as in the left A left to right shunt at caval or atrial level occurs and results in a physiological situation similar to that found in atrial septal defect with which it is not infrequently associated In isolated cases the shunt is relatively small and the condition may be only recognised as a result of a routine skiagram (fig 8 34) The anomalous vessel is commonly dilated and shows up well in tomograms (fig 8 35) A cardiac catheter may enter such a vessel directly from the superior vena cava (fig 8 36) inferior vena cava or right atrium and may be filled with contrast medium so that its course may be seen more clearly or



(a) Anterior view



(b) Lateral tomogram

Fig 8 35—Anomalous right pulmonary venous drainage into the azygos vein

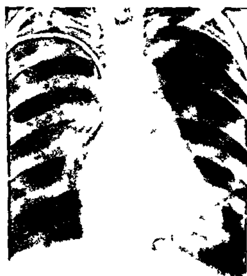


Fig 8 36—Skiagram showing a catheter lying in an anomalous pulmonary vein joining the superior vena cava

diaginol may be injected directly into the pulmonary artery through a No 9 catheter so as to delineate the whole course of the vessel

When anomalous pulmonary venous drainage is associated with atrial septal defect it may be important to know how much blood is being shunted through each If the anomalous vein joins the azygos or either vena cava this can be learned easily enough by analysing samples obtained from the vena cava above and below the entrance of the vessel and from the right atrium if it joins the right atrium however the shunt is more difficult to estimate but comparison of time concentration curves recorded by means of an ear oximeter after the injection of 30 mg of Evans blue dye first into one pulmonary artery and then into the other may help when the injection is made on the side of the anomalous pulmonary veins the left to right shunt is greater than when it is made on the contralateral side and the quantitative difference between the two curves represents the magnitude of the venous shunt

TREATMENT

It is rarely necessary to interfere with partial anomalous pulmonary venous drainage because the shunt carried is usually too small to cause any trouble and the prognosis excellent (Smith 1951) Transplantation may have to be considered however in exceptional cases and if there is a suitable pulmonary vein on the same side direct venous anastomosis can be performed

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect commonly refers to an isolated defect of the membranous part of the interventricular septum due to failure of the aortic septum to fuse with the ventricular septum Diagnosed clinically for the first time by Roger (1879) the lesion has been said to account for 35 to 37 per cent of all cases of congenital heart disease recognised at school age (Perry 1931 Muir and Brown 1934) Such high figures probably include many instances of aortic stenosis simple pulmonary stenosis infundibular stenosis and mitral *incompetence*

NOMENCLATURE

The term maladie de Roger, if used at all, should be reserved for those mild cases of ventricular septal defect that conform to Roger s original description, i e to about one third of pure uncomplicated cases (Wood Magidson and Wilson 1954) The remainder have so many characteristic features denied by this description that they have no right to the title Nor is Taussig s classification of ventricular septal defect into high (severe) and low (mild) types justified for in 90 per cent of cases the defect whether

severe or mild is located in the anterior part of the membranous septum (Selzer 1949)

INCIDENCE

In the author s series of 900 virtually proved cases of congenital heart disease ventricular septal defect occurred in its pure uncomplicated form in 8 per cent as part of Eisenmenger s complex in 3 per cent in association with simple pulmonary stenosis in 1 3 per cent and as part of Fallot s tetralogy or pulmonary atresia in 12 7 per cent thus in one form or another ventricular septal defect was found in one quarter of all cases The present section deals only with uncomplicated ventricular septal defect

The sex ratio in this series was equal, as it was in the 92 post mortem cases mostly collected from the literature by Selzer (1949)

The average age of the 72 cases described here was 12 7 years and the percentage in each decade as follows

0–10	11–20	21–30	31–40	41–50	51–60 years
51	31	10	5	2	1

HÆMODYNAMICS

During systole from the shutting of the mitral and tricuspid valves to well after aortic valve closure the high pressure gradient across the ventricular septum ensures a left to right shunt The extra quantity of blood received by the right ventricle is pumped into the lungs and is received in due course by the left atrium and left ventricle Thus both ventricles and the left atrium do more than their normal share of work only the right atrium being spared As in atrial septal defect the pulmonary vascular resistance usually remains normal so that the pulmonary blood pressure only rises when the pulmonary blood flow approaches or exceeds 15 litres per minute (hyperkinetic pulmonary hypertension) The systemic output is maintained as near to normal as possible and the arterial blood is adequately saturated with oxygen

CLINICAL FEATURES

Symptoms

Cases of mild or moderate severity have no symptoms but when the shunt is considerable patients are usually under developed and may complain of breathlessness palpitations and recurrent attacks of bron chitis In severe cases congestive failure must be expected sooner or later and is not infrequent in childhood (Marquis 1950)

Physical signs

The *facies* is normal or lean never bloated By definition all uncom plicated cases are acyanotic

The *peripheral pulse* is small when the shunt is relatively large normal in the maladie de Roger

The *jugular venous pressure and pulse* are normal unless there is heart failure

A *hyperdynamic left ventricular thrust* at the apex beat and a *lift over the right ventricle* near the left sternal border can both be felt as a rule and pulsation over the pulmonary artery in the second left space occurs in a quarter of the cases Only in the maladie de Roger is the cardiac impulse normal

Roger (1877) accurately described the *characteristic murmur* as surprisingly loud extending right through systole covering both heart sounds

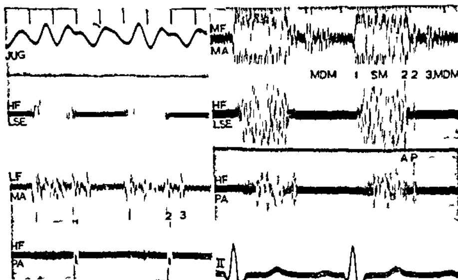


Fig 8 37—Phonocardiogram illustrating the pansystolic murmur of V S D with a simultaneous jugular phlebogram

Fig 8 38—Phonocardiogram showing a functional mitral diastolic murmur (top tracing) in a case of V S D

H F high frequency M F medium frequency L F low frequency L S E left sternal edge M A mitral area P A pulmonary area

1 k uledg ent 1 D 1 b y L th m

and with its maximal intensity over the upper third of the precordial region and chiefly median This loud pansystolic murmur (figs 8 37 and 8 38) was heard in 95 per cent of the present series usually in the 3rd and 4th left spaces near the sternal edge and was accompanied by a *thrill* in four fifths of them The murmur was soft in 3 per cent and absent altogether in 2 per cent A functional *mitral diastolic murmur* (fig 8 38) indistinguishable in timing quality intensity and duration from the Carey Coombs murmur of active rheumatic carditis was heard in precisely half the cases This murmur was noted by Laubry and Pezzi (1921) and may be attributed to a torrential mitral blood flow (Wood 1950) It is present in 90 per cent of severe cases 60 per cent of those with moderate shunts and 10 per cent of mild cases (Wood *et al* 1954) A *Graham Steell*

murmur due to functional pulmonary incompetence was heard in 14 per cent chiefly in those with pulmonary hypertension

The *second heart sound* when not obscured by the murmur is split normally or rather closely the pulmonary element is only accentuated in those with pulmonary hypertension The third heart sound is usually accentuated owing to rapid ventricular filling (fig 8 37)

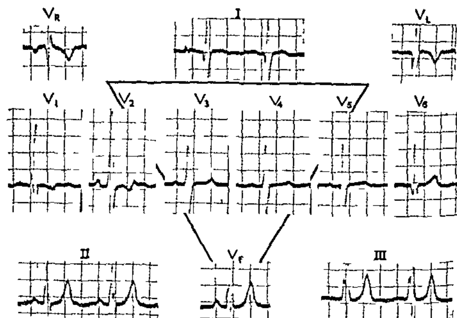


Fig 8 39—Electrocardiogram in a case of V S D showing an RSR complex in lead V_1 indicating right ventricular dilatation and a conspicuous Q wave in leads V_6 and V_L pointing to a powerful left ventricle as well

Electrocardiogram

The electrocardiogram is normal in the maladie de Roger In those with moderate or large shunts the appearances vary according to the pulmonary vascular resistance when this is low good Q waves and large R waves in leads V_5 and V_6 with or without depression or inversion of T or U and deep S waves in leads V_1 and V_2 confirm the left ventricular enlargement and dominance the pattern resembling that seen in patent ductus when the resistance is raised however a conspicuous secondary R wave is seen in lead V_1 and a terminal S wave in lead V_6 the graph resembling that seen in atrial septal defect In the majority of cases however a variable mixture of these two types of graph is seen good Q waves in leads V_5 and V_6 emphasising the presence of a vigorous left ventricle and secondary R waves in lead V_1 proclaiming right ventricular enlargement as well (fig 8 39)

Skiagram

In mild cases the appearances are normal (fig 8 40) In the majority however radiology reveals a small aorta a variable degree of dilatation of the pulmonary artery and its two main branches (with or without hilar dance), pulmonary plethora hyperdynamic enlargement of both ventricles and slight dilatation of the left atrium (fig 8 41)

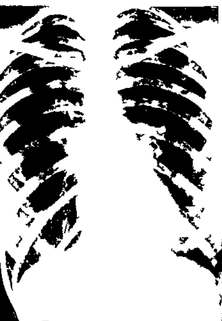


Fig 8.40—Maladie de Roger—X ray appearances



Fig 8 41—Skiagram of a case of ventricular septal defect with considerable increase of pulmonary blood flo

Differential diagnosis

The maladie de Roger is frequently confused with mild pulmonary valve stenosis simple infundibular stenosis acyanotic Fallot s tatralogy mild aortic stenosis and innocent left parasternal murmur whatever that may be

Mild pulmonary valve stenosis should be distinguished by the higher position of the thrill and murmur wide splitting of the second sound and poststenotic dilatation of the pulmonary artery

Mild infundibular stenosis with its low thrill and murmur and normal pulmonary artery is very difficult to distinguish from the maladie de Roger unless delayed pulmonary valve closure can be recognised

Acyanotic Fallot s tetralogy usually causes moderate effort intolerance even squatting in some cases and a clear single second heart sound in all other respects it may closely resemble maladie de Roger

Mild aortic stenosis should be recognised by the aortic ejection click and by the geography and timing of the aortic systolic murmur (q v)

murmur due to functional pulmonary incompetence was heard in 14 per cent chiefly in those with pulmonary hypertension

The *second heart sound* when not obscured by the murmur is split normally or rather closely the pulmonary element is only accentuated in those with pulmonary hypertension The third heart sound is usually accentuated owing to rapid ventricular filling (fig 8 37)

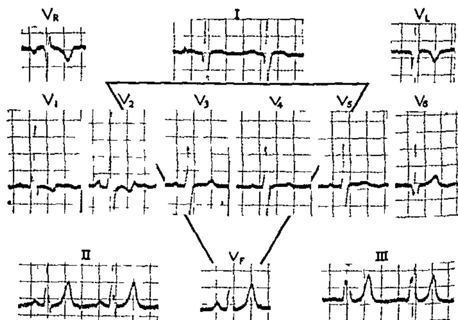


Fig 8 39—Electrocardiogram in a case of V S D showing an RSR complex in lead V_1 indicating right ventricular dilatation and a conspicuous Q wave in leads V_4 and V_L pointing to a powerful left ventricle as well

Electrocardiogram

The electrocardiogram is normal in the maladie de Roger In those with moderate or large shunts the appearances vary according to the pulmonary vascular resistance when this is low good Q waves and large R waves in leads V_5 and V_6 with or without depression or inversion of T or U and deep S waves in leads V_1 and V_2 confirm the left ventricular enlargement and dominance the pattern resembling that seen in patent ductus when the resistance is raised however a conspicuous secondary R wave is seen in lead V_1 and a terminal S wave in lead V_6 the graph resembling that seen in atrial septal defect In the majority of cases however a variable mixture of these two types of graph is seen good Q waves in leads V_5 and V_6 emphasising the presence of a vigorous left ventricle and secondary R waves in lead V_1 proclaiming right ventricular enlargement as well (fig 8 39)

roved at operation and in consideration of the technical errors involved in sampling it is clear that defects measuring less than 2 mm in diameter and passing shunts of less than 1 litre per minute would not be detected with ordinary routine methods of investigation It must be admitted therefore, that a pansystolic left parasternal murmur with entirely normal physiological findings could well be due to a minute ventricular septal defect for necropsies have certainly proved the existence of such minute defects This does not mean however that the maladie de Roger is common after all because the majority of cases so labelled on traditional evidence have been proved by modern techniques to have a different explanation for the murmur

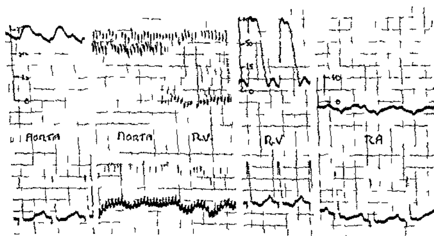


Fig 8 42—Pressure pulses from a case of ventricular septal defect with hyperkinetic pulmonary hypertension at systemic level the pulmonary blood flow was 20 L min and the resistance 3 units

In one third of the mild cases there was a significant difference between infundibular and low right ventricular samples the former resembling samples from the pulmonary artery the latter samples from the right atrium this difference was very rarely found in moderate or severe cases

The pulmonary vascular resistance was raised moderately in half the severe cases There is good evidence that the size of the defect is not directly responsible for the behaviour of the small pulmonary vessels in these instances (see Eisenmenger s complex) but it was never smaller than the critical 1 cm in diameter Severe cases without a raised resistance are apt to die of left ventricular failure or bronchopneumonia in childhood for there is then little to prevent an intolerable shunt The pulmonary blood pressure alone gives little indication of the resistance and may even reach systemic level when the resistance is normal if the shunt is large enough (fig 8 42) This may be called hyperkinetic pulmonary hypertension

COMPLICATIONS

Eisenmenger's complex (q v), which may be defined as pulmonary hyper tension with bidirectional or reversed interventricular shunt usually occurs when the pulmonary vascular resistance lies between 10 and 20 units

Complete heart block occurred in only one of the 72 cases recorded here Conversely when ventricular septal defect had been diagnosed elsewhere in several cases of congenital heart block no shunt could be demonstrated by means of cardiac catheterisation and careful auscultation supported by phonocardiography usually proved that the systolic murmur on which the diagnosis had been based was in fact an aortic or pulmonary ejection murmur Functional mitral incompetence may also mislead

Bacterial endocarditis was the cause of death in 22 per cent of the 80 necropsied cases reviewed by Selzer (1949) Its true incidence is difficult to assess frequency rates as high as 57 per cent being recorded in post mortem material (Gelfman and Levine 1942 Welch and Kinney 1948) and as low as 1 per cent in clinical series (Perry 1937 Muir and Brown 1934 Wood *et al* 1954) perhaps 10 to 20 per cent would be near the truth Vegetations form on the right ventricular side of the septum around the defect and on the opposite wall of the right ventricle where the shunted blood stream impinges Emboli are confined to the pulmonary circulation and may cause subacute or recurrent hæmorrhagic pulmonary inflam mation or infarction

Pulmonary or infundibular stenosis with normal aortic root and left to right shunt may be associated with ventricular septal defect (Abrahams and Wood 1950) the combination occurring in 1 5 per cent of all cases of congenital heart disease (Wood *et al* 1954) When the stenosis is mild it is usually overlooked until demonstrated by means of cardiac catheterisation when it is relatively severe the ventricular septal defect is usually over looked clinically Cases with bidirectional or reversed shunt are indistin guishable from Fallot s tetralogy

Aortic incompetence the anterior cusp being prolapsed into the defect (fig 8 43) or tethered towards the defect by a fibrous band (Laubry and Pezzi 1921) occurs in about 2 per cent of cases (Wood Magidson and Wilson 1954) The combination may be mistaken for patent ductus and so lead to fruitless thoracotomy

PROGNOSIS

During the seven year period in which these 72 cases of isolated un complicated ventricular septal defect have been studied none have died of the lesion But there were only three patients over 40 years old whereas 15 5 per cent of patients with atrial septal defect were over 40 Again 29 per cent of 88 fatal cases collected by Selzer (1949) died during the first year of life and another 20 per cent between the ages of 1 and 5 The

average age of death in Abbott's series was 14, the oldest being 49. It is clear, therefore, that ventricular septal defect is a serious anomaly, patients often dying from congestive failure in early childhood (Baldwin, Moore and Noble, 1946), and it is only the mild maladie de Roger that has a good prognosis. The only risk in these mild cases is bacterial endocarditis, and with modern treatment this can usually be cured.

There have been some interesting cases in which characteristic signs of a ventricular septal defect discovered in childhood have disappeared with advancing years. Whilst it is difficult to prove that these were not examples of innocent left parasternal murmur, it has been suggested that spontaneous obliteration of small defects may sometimes occur (Parkes Weber, 1918).

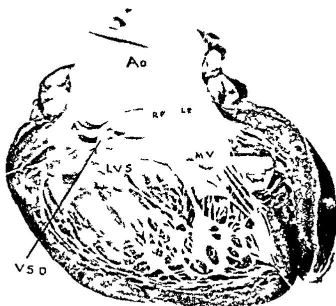


Fig. 8.43—Photograph of specimen from a case of aortic incompetence complicating V.S.D.: the anterior aortic cusp is prolapsed into the defect.

[illegible] Dr. Reginald H[illegible]

TREATMENT

No reparative treatment is yet available, but Murray (1948) first made the attempt. Mild cases should be encouraged to lead normal unrestricted lives, but severe cases need care and should limit their physical activities. Dental treatment, sore throat and other pyogenic infections should be covered by a short course of penicillin to prevent endocarditis.

PATENT DUCTUS ARTERIOSUS

EMBRYOLOGY

In fœtal life the ductus arteriosus joins the root of the left pulmonary artery to the aorta at a point immediately distal to the left subclavian artery and it is a short muscular vessel 1 cm or so in length and about as wide as the great vessels which it joins In the unaerated lung of the fœtus the pulmonary capillaries and arteries are practically shut down and offer a resistance to flow that is much higher than the systemic resistance mixed venous and placental blood from the right ventricle therefore passes directly from the pulmonary artery into the descending aorta At the same time mixed venous and placental blood which has passed through the foramen ovale is pumped by the left ventricle into the ascending aorta Although further mixing undoubtedly takes place in the arch of the aorta on the whole left ventricular blood passes to the head and upper extremities while right ventricular blood passes to the trunk and lower extremities It should be clearly understood that the systolic pressures in the two ventricles and great vessels are identical the ventricles are subjected to the same filling pressure and work against the same total peripheral resistance

At birth aeration of the lung is followed by a rapid decline in pulmonary vascular resistance alveolar oxygenation discouraging pulmonary vaso constriction Within three hours of birth blood sent to the right arm is over 90 per cent saturated with oxygen whereas blood sent to the legs is still partly venous from the end of the third hour the pulmonary vascular resistance gradually falls below systemic level the process being completed in normal individuals by the end of the third day after which arterial samples from the arms and legs are the same (Eldridge Multgren and Wigmore 1954) The duct itself normally closes by some inherent process within the first six weeks after birth

INCIDENCE

Patent ductus was the chief or sole lesion in 9 2 per cent of Abbott's 1 000 collected cases of congenital heart disease and accounted for 13 per cent of my own 900 an additional 2 per cent having reversed shunt

The sex ratio is 7 3 in favour of females (Gross 1952) there were 78 females and 37 males in the present series

In the 115 cases reported here the average age was 17 and the percentage distribution per decade as follows

Age	0–10	11–20	21–30	31–40	41–50	51–60
No per cent	36	32	15	9 5	6 5	1

HÆMODYNAMICS

Since the systemic peripheral resistance is normally about eight times the pulmonary, the shunt in uncomplicated patent ductus is from aorta to pulmonary artery The total systemic resistance is lowered by the leak from the aorta arterial blood enters the pulmonary circulation the total

pulmonary blood flow is increased and the left atrium and left ventricle have to deal with the augmented flow the total blood volume is raised (Cassels and Morse, 1947) Hyperkinetic pulmonary hypertension may occur with large shunts as with atrial septal defect and ventricular septal defect but the pulmonary vascular resistance is not ordinarily raised High pulmonary resistances around 15 units (systemic level) occur in 10 to 15 per cent of cases and may result in reversed shunt (see Eisenmenger s syndrome) Included in the present section is a small group (7 per cent) in which the pulmonary resistance is moderately raised but insufficiently so to prevent a predominant aorto pulmonary shunt

CLINICAL FEATURES

There are no symptoms in mild or moderate cases In severe cases with large shunts recurrent bronchitis and bronchopneumonia are common in childhood as with severe atrial septal defect and ventricular septal defect Physical development is usually poor palpitations and throbbing may be troublesome and there may be symptoms of left ventricular failure

Physical signs

The *peripheral pulse* is water hammer in quality Corrigan s sign may be present in the neck and the diastolic blood pressure tends to be low according to the degree of aorto pulmonary shunt

The *venous pressure* is normal in uncomplicated cases but may be raised a little if the pulmonary vascular resistance is high or as a result of an increased blood volume

The *cardiac impulse* is left ventricular in type and hyperdynamic Medial retraction over the right ventricle confirms that the left ventricle is alone enlarged Pulsation in the second left space over the pulmonary artery may be appreciated when the shunt is large or when there is a raised pulmonary vascular resistance

On *auscultation* the chief sign is the classical machinery murmur of Gibson (1900) it is usually heard best in the first or second left interspace is more or less continuous waxes towards the end of systole wanes in mid diastole and is accompanied by a thrill in two thirds of cases It may be absent in infancy although it has been recorded as early as the sixth week (Adler 1953) This typical murmur was heard in 95 per cent of the present series The murmur was systolic only in two cases with gross shunt in one trivial case and in two with a raised pulmonary vascular resistance which was insufficient to prevent an aorto pulmonary shunt A continuous murmur was never heard in the pulmonary hypertensive cases with reversed shunt In difficult ca es a doubtful Gibson murmur may be brought out by any device that increases total flow (such as exercise) or that increases the pressure gradient across the duct (such as Muller s experiment)

The *second heart sound* was usually difficult to analyse clinically in view of the loud coincident bruit but phonocardiography showed that aortic

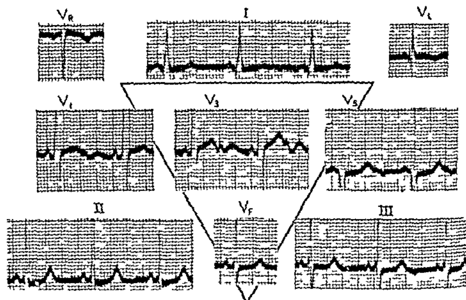


Fig 8 44—Electrocardiogram in a case of patent ductus showing left ventricular enlargement There is a strong QR pattern with inverted U waves in lead V5

valve closure was delayed in cases with large shunt A often falling after P the split being reversed (Gray 1955) The phenomenon was attributed to delayed emptying of an overfilled left ventricle

A *pulmonary diastolic murmur* due to functional pulmonary incompetence was recognised in 8 per cent In the group with pulmonary hypertension and reversed shunt (discussed later) it was heard in 70 per cent

A *functional mitral diastolic murmur* due to a torrential mitral blood flow was detected in 39 per cent of all uncomplicated cases it was present in 87 per cent of those with large shunts and in one third of those with

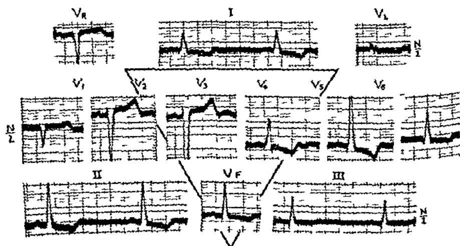


Fig 8 45—Gross left ventricular preponderance in a case of patent ductus

moderate shunts but never in mild or trivial cases It commonly disappeared after ligation of the duct this rapid flow murmur was never heard in the true pulmonary hypertensive group

Electrocardiogram

The electrocardiogram is normal in mild cases and usually normal in cases of moderate severity but when the shunt is large prominent Q waves unusually tall R waves and perhaps inverted U waves in leads V and V_6 confirm the enlargement of the left ventricle (fig 8 44) and in the most florid cases the T waves may be inverted in left ventricular surface leads or their equivalents (fig 8 45) In striking contrast to atrial septal defect no case of patent ductus had a partial right bundle-branch block pattern

Radiological appearances

Skiagrams (figs 8 46 and 8 47) reveal pulmonary plethora dilatation of the pulmonary artery enlargement of the left ventricle and slight dilatation of the left atrium (Donovan Neuhauser and Sosman 1943) A conspicuous hilar dance is unusual and the right branch of the pulmonary artery is rarely impressive The aorta in patent ductus is not so small (fig 8 48) as in atrial septal defect and ventricular septal defect and may be more pulsatile The right ventricle and atrium are strictly normal in uncomplicated cases Rarely a comma shaped arc of calcium can be seen in the ductus or in the wall of the left pulmonary artery opposite to the opening of the ductus

A local bulge in the region of the aortic isthmus can be demonstrated by means of angiocardiography in a limited number of cases and is thought to represent the widened mouth of the ductus or possibly a traction aneurysm of the aorta (Steinberg Grishman and Sussman 1943) A characteristic filling defect at the top of the left pulmonary artery has been described by Goetz (1951) With suitable technique angiocardiograms may also show the pulmonary artery filling twice first from the right ventricle then from the aorta Retrograde aortography offers an alternative means of obtaining good angiograms



Fig 8 46—Skiagram of a case of patent ductus showing enlargement of the left ventricle but little dilatation of the pulmonary artery



Fig 8 47—Skiagram of a more advanced case of patent ductus showing considerable left ventricular enlargement and engorgement of the pulmonary vessels in addition to dilatation of the pulmonary artery

PHYSIOLOGICAL FINDINGS

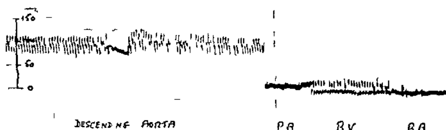
The diagnosis may be proved in doubtful cases by means of cardiac catheterisation Samples of blood from the superior vena cava right atrium and right ventricle are normal (about 70 per cent saturated) whereas samples from the pulmonary artery are usually 80 to 85 per cent saturated Slight admixture of arterial blood in right ventricular samples may be found when there is functional pulmonary incompetence



Fig 8 48—Skiagram of a case of patent ductus showing a prominent aortic knuckle in addition to dilatation of the pulmonary artery and pulmonary plethora

In the present series 61 cases were catheterised about a third of them in each group of severity In mild cases the pulmonary blood flow measured about 1 5 times the systemic flow and in three instances no shunt at all could be demonstrated even in one catheterised twice At operation in these mild cases the duct did not exceed 0 6 cm in external diameter

In the moderate group the pulmonary blood flow was 2 to 2½ times the systemic flow being commonly around 10 to 12 litres per minute The pulmonary blood pressure and vascular resistance were normal (fig 8 49) and at operation the duct usually measured from 7 to 12 mm in external diameter



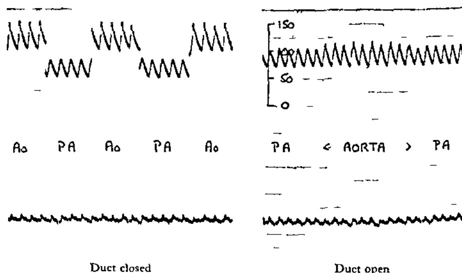
Time marking 1 and 5 sec

Fig 8 49—Pressure pulses from the descending aorta and pulmonary artery in an uncomplicated case of patent ductus showing a steep pressure gradient between the two

In the severe cases with normal resistances the pulmonary blood flow averaged 3 5 times the systemic flow ranging between 12 and 30 litres per minute Hyperkinetic pulmonary hypertension was demonstrated in

all but two of these cases the average pressure being 55/35 mm Hg and the range from 32/15 to 75/55 The pulmonary vascular resistance was normal averaging 2 units, the range being 0 5 to 4 The pulmonary blood pressure never quite reached systemic level at rest in this group but approached it very closely in several instances as a result of temporary stress and would presumably do so also on exercise At operation the duct was always more than 1 cm in external diameter

The arterial oxygen saturation was normal for catheter conditions (90 to 97 per cent) in 88 per cent of all these cases and between 87 and 89 per cent in the remainder



Duct closed

Duct open

Time marking 0 2 and 1 0 sec

Fig 8 50—Case of patent ductus with hyperkinetic pulmonary hypertension together with a moderately raised pulmonary vascular resistance when the ductus was open the pulmonary artery pressure was 10 mm Hg lower than the aortic when the ductus was closed the aortic pressure rose from 115 to 150 mm Hg and the pulmonary artery pressure fell from 105 to 83 mm Hg

Finally there was a small group (5 per cent) of severe cases in which the pulmonary vascular resistance was raised (5 to 9 units) but in which the shunt was still unidirectional or predominantly from aorta to pulmonary artery Although the ductus itself was about 1 cm in diameter the raised resistance prevented a large shunt the average pulmonary blood flow being barely twice the systemic flow The pulmonary blood pressure was more or less at systemic level (fig 8 50) These cases are not yet in the Eisenmenger group but could become so

By repeatedly guiding the tip of the catheter from the left to the right pulmonary artery and back again the ductus was sooner or later entered in one third of the last 42 cases catheterised As it passes through the duct the catheter lies at the level of the left pulmonary artery, with the sub aortic window above it (fig 8 51) The tip nearly always passes straight

down the descending aorta very rarely into the left subclavian artery When a catheter passes through an aorto pulmonary window its course up the ascending aorta and round the arch is higher as can be demonstrated by superimposing on the skiagram a second film with the catheter lying in the left pulmonary artery Again in the anterior view a catheter passing through a duct and down the descending aorta usually curves backwards in a medial direction (fig 8 63) whereas a catheter passing up the ascending aorta and round curves backwards in a left lateral direction (fig 8 101) in other words the former tends to loop anticlockwise the latter clockwise



Fig 8 51—Skiagram in the second oblique position showing a catheter passing through a patent ductus down the descending aorta the sub aortic window lies above the catheter

DIFFERENTIAL DIAGNOSIS

Errors in the diagnosis of patent ductus arteriosus fall into four main groups

1 *Mistaking other continuous murmurs for Gibson s murmur*

A *jugular venous hum* can be abolished at once by compressing the jugular veins at the root of the neck

Pulmonary atresia with a broncho pulmonary anastomosis may cause a continuous murmur on either or both sides but such cases are cyanotic and patent ductus with reversed shunt causing cyanosis loses the Gibson murmur

Arterio venous fistula in the left upper lobe of the lung may cause a continuous murmur under the left clavicle but the skiagram should reveal the opacity and if the lesion is of any size there should be central cyanosis *Coronary arterio venous fistula* causes a machinery murmur at a lower level and the skiagram may show a calcified aneurysm *A congenital arterio venous angioma* in the thoracic wall is very rare and unlikely to be in the right place to cause confusion

Perforation of an aortic sinus into the pulmonary artery secondary to bacterial endocarditis and therefore usually with aortic incompetence as well may be very confusing In the only case I have seen, which was presented to me as a recanalised duct (for the [illegible] and the ligamentum arteriosum ligated) the gross water [illegible] blood

pressure 180/40) and greatly enlarged and hyperdynamic left ventricle were out of proportion to the relatively slight degree of pulmonary plethora and the 2 1 shunt demonstrated by cardiac catheterisation

An *aorto pulmonary septal defect* is clinically indistinguishable from patent ductus, for physiologically it is identical It is likely to be encountered in 1 to 2 per cent of all cases submitted for ligation The machinery murmur may be exceptionally loud and perhaps a little low and central but little confidence can be placed on minor differences of this kind If a catheter can be passed through the communication its course may settle the question failing that retrograde aortography or selective dye concentration curves may solve the problem But on the whole it may be more economical to accept the slight risk of diagnostic error and to proceed as if any aorto pulmonary shunt were due to patent ductus for such an assumption will save 98 patients out of 100 much discomfort Aorto pulmonary septal defects may themselves be repaired but require the help of hypothermia or some form of temporary artificial circulation

2 *Mistaking certain combinations of murmurs for Gibson s murmur*

Ventricular septal defect with aortic incompetence has often been mistaken for patent ductus not only because the combined murmurs have been misinterpreted but also because of the water hammer pulse predominant hyperdynamic left ventricle functional mitral diastolic murmur and pulmonary plethora Nevertheless this is an error that should not be made for the two or three murmurs present do not make the Gibson murmur and the degree of water hammer pulse and left ventricular enlargement are disproportional to the amount of plethora

Combined mitral and aortic incompetence in children without a rheumatic history may also confuse experienced cardiologists again because the combination of murmurs superficially resembles the Gibson murmur and because of the water hammer pulse predominant and hyperdynamic left ventricle and short mitral diastolic murmur But there is no pulmonary plethora—only pulmonary venous congestion—and the murmurs should not really be mistaken for Gibson s murmur

3 *Mistaking other members of the plethoric group for patent ductus*

The difficulty here is only encountered in relation to patent ductus without a continuous murmur The syndrome includes a pulmonary systolic murmur perhaps a Graham Steell murmur a hyperdynamic enlarged left ventricle a functional mitral diastolic murmur and pulmonary plethora Possible causes include ventricular septal defect patent ductus and persistent truncus A small pulse right ventricular dilatation as well as left pansystolic murmur close but normal splitting of the second sound and diminutive aorta favour ventricular septal defect Central cyanosis of course at once distinguishes persistent truncus but failing that there is still the loud single second sound and the prominent

aorta Patent ductus without a continuous murmur is suggested by a water hammer pulse pure left ventricular enlargement and reversed splitting of the second sound

Despite these considerations real difficulty in accurate bedside diagnosis often arises and is not always resolved by means of cardiac catheterisation although theoretically the physiological data should be conclusive

Difficulty with the Eisenmenger syndrome

Cases with pulmonary hypertension due to an extreme pulmonary vascular resistance (average 17 units) and reversed aorto pulmonary inter ventricular or interatrial shunt are very difficult to sort out at the bedside and will be discussed fully later (see Eisenmenger s syndrome) For tunately at the present time the distinction between these three conditions is purely academic

ASSOCIATED ANOMALIES AND COMPLICATIONS

Although patent ductus may be associated with almost any other con genital anomaly in clinical practice it usually occurs alone the more common associated lesions include *coarctation of the aorta* as already described and *tricuspid atresia* In the latter the ductus serves a useful purpose by providing a natural pathway whereby mixed venous and arterial blood can reach the lungs Patent ductus is remarkably rare in any form of pulmonary stenosis and I have not so far encountered it in other wise uncomplicated atrial septal defect

Patent ductus may be associated by chance with certain acquired con ditions such as rheumatic mitral valve disease and essential hypertension Organic *mitral incompetence* is seriously aggravated by the increased left ventricular stroke volume resulting from the shunt and provides a strong reason for ligating the ductus without delay although the result may be disappointing if the incompetence is already severe The effects of *mitral stenosis* are also seriously aggravated by the increased pulmonary blood flow resulting from the shunt and the combination calls for urgent surgical treatment mitral valvotomy and ligation of the ductus may be undertaken at the same operation In view of the serious consequences of coincident patent ductus and mitral valve disease active rheumatic carditis itself constitutes an important indication for advising early ligation *Essential hypertension* increases the aorto pulmonary shunt through a patent ductus and therefore puts a double load on the left ventricle on the other hand the aorto pulmonary communication lowers the total systemic resistance and tends to check the rise of blood pressure It is probably best to advise ligation of the ductus in these rare cases and to treat the increased hypertension that results by medical means

True complications of patent ductus include bacterial endarteritis heart failure functional mitral incompetence and pulmonary hypertension These are all discussed elsewhere

PROGNOSIS

An appreciable number (perhaps 20 to 25 per cent) of cases of patent ductus die from left ventricular failure in infancy (Ziegler 1952) The average age of death was 24 in Abbott s post mortem series (1932) and 36 in a group of 60 cases reported by Shapiro and Keys (1943) The lesion is therefore not as benign as might be supposed The maximum age of survival so far recorded is 75 (Fishman and Silverthorn, 1951) The chief dangers are bacterial endarteritis and congestive heart failure Bacterial endarteritis occurred in 30 per cent of Abbott s series and in 37 5 per cent of those who survived early childhood Vegetations appear first at the pulmonary end of the ductus or on the opposite wall of the left pulmonary artery Spread to the heart valves (pulmonary aortic or mitral) occurs in 75 per cent of untreated cases (Vesell and Kross 1946)

Congestive heart failure occurred in 32 per cent of Abbott s 73 cases that survived infancy and in 30 per cent of 60 cases reported by Shapiro and Keys (1943) The gloomy prospects suggested by these reports are not entirely valid however for cases that come to necropsy are highly selected Clinical studies on unselected cases of patent ductus indicate a more favourable prognosis Thus Wilson and Lubschez (1942) followed 38 cases for an average period of 20 years during which there were no deaths from bacterial endocarditis or congestive failure Again Benn (1947) followed 30 cases for an average period of 8 years without meeting a single complication

TREATMENT

Radical cure first achieved by Gross and Hubbard (1939) consists of ligation of the ductus or of excision of the ductus between ligatures and has proved very effective (figs 8 52 and 8 53) The most favourable age is between 6 and 10 Surgical treatment not only prevents bacterial endocarditis but usually cures this complication after its development (Touroff and Vesell 1940 Vesell and Kross 1946) Recanalisation is rare The total operative mortality is now 2 per cent and in uncomplicated cases only 0 5 per cent (Gross 1947 Crafoord 1948 Gross and Longino 1951) Of the author s cases 60 have so far been operated on without a death Bacterial endocarditis should be cured by means of penicillin if possible before submitting the patient to operation

Selection of cases for surgical treatment

Infants with large shunts should have the ductus ligated and divided if possible without delay for the risk of early death from heart failure is considerable (Ziegler 1952) Indeed *all patients with large shunts* should be operated on without delay whatever the age at least up to the sixth decade

A *moderately raised pulmonary vascular resistance* (5 to 9 units) is a strong indication for surgical treatment for if the duct is not ligated the resistance



Fig 8 52—Case of patent ductus with large shunt

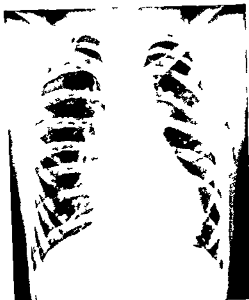


Fig 8 53—Same case one year after ligation

may be expected to reach systemic level sooner or later when it would be too late to help Surgery is contra indicated when the shunt is prevented or reversed by a pulmonary vascular resistance over 10 units Continued disregard for this rule has resulted in many deaths from unrelieved pulmonary hypertension then and there or within a year of the operation for without the duct there is no safety valve in the pulmonary circulation and the physiological situation becomes similar to that in primary pulmonary hypertension It is unreasonable to expect the resistance to fall after ligating the ductus when the pulmonary blood flow is already normal or diminished Surgery may still be advised however in cases of bi directional shunt if the pulmonary blood flow is increased

Bacterial endarteritis past or present provides strong grounds for ligation for infection is likely to be recurrent and on the next occasion may well prove fatal or do untold damage before being brought under control by means of antibiotics If bacterial endarteritis does not respond to medical treatment the operation should not be delayed for closure of the ductus alone cures the infection in two thirds of cases (Tubbs, 1944)

The only remaining question is whether or not to advise ligation in uncomplicated cases of mild or moderate degree In this group the surgical mortality is 0 5 per cent and the risk of subsequent bacterial endarteritis not less than 10 per cent at the most conservative estimate Since at least one fifth of cases of bacterial endocarditis prove fatal it follows that the immediate surgical risk is four times less than the ultimate risk of con servative management It is believed that this is not offset by the significant

difference between the words *immediate* and *ultimate* and that therefore all uncomplicated cases of patent ductus should be operated on, at least up to the age of 50 years

EISENMENGER'S SYNDROME OR PULMONARY HYPERTENSION WITH REVERSED SHUNT

DEFINITION

Eisenmenger's complex is ventricular septal defect with reversed shunt in the absence of pulmonary stenosis (Eisenmenger 1897) Until quite recently the reversed shunt was attributed to displacement of the root of the aorta to the right its position astride the defect seeming to favour reception of blood from both ventricles Eisenmenger himself was not responsible for this misconception and thought that any apparent over ride demonstrated at necropsy could be the result rather than the cause of the reversed shunt (Eisenmenger 1898) It is now known that the essential cause of the altered physiology in cyanotic cases of ventricular septal defect without pulmonary stenosis is a pulmonary vascular resistance more or less at systemic level The definition of Eisenmenger's complex therefore becomes *pulmonary hypertension with reversed interventricular shunt* Whether the aorta appears to ride over the defect or not is physiologically irrelevant

At the bedside and after viewing the electrocardiogram and skiagram it is usually easy enough to make a diagnosis of pulmonary hypertension with reversed or bidirectional shunt but often extremely difficult or impossible to determine the level of the shunt The term Eisenmenger syndrome has been used to describe this clinical picture (Wood 195) reserving the title Eisenmenger's complex to define a reversed shunt at ventricular level and there is something to be said for this attitude Alternatively the group as a whole might be called pulmonary hypertension with reversed shunt leaving the site of the shunt unspecified

HÆMODYNAMICS

When the pulmonary vascular resistance is less than the systemic blood flows through a patent ductus or ventricular septal defect from left to right when the resistances are the same there may be no shunt at all and when the pulmonary resistance is higher the shunt is reversed This general law is not absolute for a shunt may occur at any time during the cardiac cycle but it is true enough as a working hypothesis To some extent it is also true for atrial septal defect although here there is obviously room for much greater variation for atrial pressures are only indirectly related to peripheral resistances

In patent ductus the reversed shunt is directed chiefly down the descending aorta so that the feet may be blue while the hands and face are pink (differential cyanosis) In ventricular septal defect and atrial septal defect with reversed shunt cyanosis is uniform

In patent ductus and ventricular septal defect with reversed shunt the systolic pressure in the pulmonary artery and right ventricle is always precisely the same as the systolic pressure in the aorta and left ventricle any potential pressure gradient between the two circulations being compensated for by the shunt flow This does not apply to atrial septal defect with reversed shunt in which the pulmonary artery pressure may be higher equal to or lower than the aortic in atrial septal defect also the pressure relationship between the two circulations may alter with changing conditions e g with exercise

When the shunt is wholly reversed the pulmonary blood flow is diminished the total systemic output remaining about normal

In patent ductus the left ventricular stroke volume is diminished by an amount equal to the shunt from pulmonary artery to descending aorta so that the right ventricle does the greater work the total resistance against which each ventricle is pumping being the same In ventricular septal defect the work of each ventricle is identical for although the left still receives a diminished amount from the left atrium its full quota is made up by the shunt at ventricular level In atrial septal defect with unidirectional reversed shunt the right ventricle pumps less blood than the left but if the pulmonary resistance is higher than the systemic it may have to do more work

On the whole the physiological situation is not bad The naturally high systemic resistance tends to prevent too great a right to left shunt at any level and so ensures a fair pulmonary blood flow at the same time the high pulmonary resistance is prevented from overburdening the right ventricle by the defect acting as a safety valve in the pulmonary circulation

The defect in Eisenmenger s complex is always 1 cm or more in diameter and *the high pulmonary resistance seems to be established at birth* Cases with ventricular septal defect of similar size in which the high fœtal pulmonary resistance falls to normal soon after birth run a serious risk of dying from heart failure in infancy It may be pointed out however that there is a well defined limit to the size of a left to right shunt when the pulmonary vascular resistance is normal the ceiling being reached when hyperkinetic pulmonary hypertension reaches systemic level Unfortunately the pulmonary blood flow has to be four to six times the systemic flow before this happens and few ventricles will tolerate such a burden It follows that in many cases the high pulmonary resistance of Eisenmenger s syndrome is life saving The ideal physiological reaction would be a pulmonary resistance of 5 to 6 units enough to ensure equalisation of pressures in the two circulations with moderate left to right shunts

Just what causes the high resistance is unknown Edwards (1950)

Civin and Edwards (1950 and 1951) originally suggested that it represented persistence of the fœtal type of pulmonary circulation in which a high resistance is maintained by thick muscular arteries, the object being to divert the blood flow from the lungs to the descending aorta via the ductus arteriosus Failure of this high resistance to subside when the lungs become aerated may be due to the hyperkinetic pulmonary hypertension that would occur at once if it did so in other words, pulmonary hypertension itself may be responsible for the vasoconstriction that maintains it Much the same idea was expressed by Soulie *et al* (1953) except that these authors blamed the riding aorta for the initial pulmonary hypertension –

INCIDENCE

Pulmonary hypertension with bidirectional or reversed shunt through a patent ductus occurred in 2 per cent through a V.S.D. in 3 per cent and through an A S D in 1.5 per cent of the author's series of 900 cases of congenital heart disease Considering the relative frequencies of these three anomalies when uncomplicated (13 per cent 8 per cent and 18 per cent respectively) it may be seen that the Eisenmenger reaction occurred in 13 3 per cent of those with patent ductus 27 2 per cent of those with V S D and 7 7 per cent of those with A S D These rather startling differences are qualitatively just what might have been expected for of the three only atrial septal defect can be of unlimited size without necessarily endangering life and there are stricter limits to the size of a patent ductus than there are to the size of a ventricular septal defect In other words most cases of large atrial septal defect do not depend on the Eisenmenger reaction for their survival and there should be relatively more cases of ventricular septal defect of the necessary critical size than cases of patent ductus Swan *et al* (1953) found the same qualitative difference between the relative frequencies of raised resistances in these three conditions with direct left to right shunts still operating and pulmonary flows averaging twice the systemic flows the mean pulmonary artery pressure was above 40 mm Hg in 41 5 per cent of cases of patent ductus 70 per cent of cases of ventricular septal defect and only 5 per cent of cases of atrial septal defect

The *sex bias* when present was much the same as in uncomplicated cases of patent ductus V S D and A S D This denies the implication of the strong female sex factor operating in primary pulmonary hypertension

SEX RATIO

	Patent ductus		*V S D*		*A S D*	
	M	F	M	F	M	F
Uncomplicated	1	2	1	1	2	3
Eisenmenger syndrome	6	10	14	14	3	11

The *average age* of the patients with Eisenmenger s syndrome was also much the same as in uncomplicated cases of patent ductus and atrial septal

defect but was older in Eisenmenger's complex proper than in simple ventricular septal defect as shown in the table

	AVERAGE AGE (years)		
	Patent ductus	*V S D*	*A S D*
Uncomplicated	17	12 7	23
Eisenmenger syndrome	16	2[illegible]	22

These figures help to show that *the high pulmonary vascular resistance of Eisenmenger's syndrome is not the end result of a direct shunt acting over a long period of time*

CLINICAL FEATURES

Life long *effort dyspnœa* had limited physical activity in all but one of these 58 cases and had changed little through the years Those with atrial septal defect were most incapacitated averaging grade 3 (considerable) effort intolerance those with patent ductus were best averaging grade 2 effort intolerance while cases with ventricular septal defect fell midway between the two A history of *squatting* was obtained in 10 per cent but in none with patent ductus

Angina pectoris occurred in 10 per cent and was encountered equally in each group These six patients were all young adults aged 21 to 36 years and were no more cyanosed at rest than those without pain

Syncopal attacks also occurred in 10 per cent again with examples in each group They were usually provoked by effort and were associated with increased cyanosis None were fatal and they seemed neither as frequent nor as dangerous as in Fallot's tetralogy No opportunity to investigate the mechanism presented itself

Recurrent hæmoptysis was as frequent as angina pectoris and syncope but not more so The best examples were in older patients with either ventricular septal defect or atrial septal defect The cause of the hæmorrhage is obscure

Central cyanosis at rest usually dating from infancy (Donzelot *et al* 1949) was almost invariable in those with V S D (95 per cent) usual in those with A S D *(75 per cent) and relatively uncommon with patent* ductus (27 per cent) Even on effort one third of those with patent ductus remained acyanotic in the head and upper extremeties over half of them (57 per cent) however showed differential cyanosis at rest the face and hands being pink and the toes blue especially in a hot bath The idea that the onset of central cyanosis is typically late in Eisenmenger's syndrome occurring first around the age of puberty perhaps could not be substantiated although minimal cyanosis in childhood may certainly become more marked with advancing years Indeed, the sudden onset of dyspnœa and cyanosis in adults with a septal defect suggests some special reason for the sudden rise of pulmonary vascular resistance the two most likely

causes being multiple pulmonary embolism (especially in relation to pregnancy) and chronic bronchitis and emphysema *Clubbing of the fingers* was similarly most common in those with V S D (92 per cent) frequent enough with A S D (60 per cent) and least common in those with patent ductus (20 per cent) Clubbing of the toes alone was seen in two cases with patent ductus *Polycythaemia* (hæmoglobin over 15 G per cent) occurred in 85 per cent of the V S D cases 75 per cent of the A S D cases and 40 per cent of those with patent ductus Thus on all three counts in Eisenmenger s syndrome ventricular septal defect was associated with the greatest shunt reversal and patent ductus with the least while atrial septal defect occupied a middle position It must be said here however that this clinical conclusion was not confirmed by catheter studies for the arterial oxygen saturation averaged 80 per cent in those with V S D and 79 5 per cent in those with A S D with patent ductus it averaged 91 4 per cent in the right brachial artery and 81 2 per cent in the descending aorta

The *peripheral pulse* was usually small in those with A S D more often normal than small in those with V S D and either small or normal with patent ductus The pulse was normal in quality in all three groups

The *blood pressure* averaged 110 80 in those with A S D and 120/80 in those with V S D and patent ductus confirming the clinical impression of a smaller pulse when the shunt was at atrial level

The *jugular venous pressure* and pulse were normal in 60 per cent of all cases *a* was dominant usually measuring 3 mm Hg above *v* in 30 per cent and a large high pressure *v* wave due to heart failure or tricuspid incompetence was seen in 10 per cent Both conspicuous *a* waves and large *v* waves were relatively more common in cases with A S D than in the other two groups Giant *a* waves measuring more than 5 mm Hg were seen in only one instance

The *cardiac impulse* was impalpable in the region normally occupied by the left ventricle in one third of those with atrial septal defect and in two thirds of the other two groups the right ventricle occupied the apex beat in two thirds of those with atrial septal defect and in one third of the other two groups There was a conspicuous left parasternal heave over the hypertrophied right ventricle in half the atrial cases and in a quarter of the others while in the remainder the lift over the right ventricle was relatively slight and was absent altogether in 10 per cent of those with V S D and patent ductus In other words the right ventricle tended to be largest when the shunt was at atrial level *Pulsation over the pulmonary artery* itself was felt in three quarters of all cases

Auscultation revealed a systolic murmur over the right ventricular out flow tract and pulmonary artery in 82 per cent of all cases With A S D and patent ductus it was always an ejection murmur and usually followed a loud pulmonary ejection click with two exceptions it was loudest in the second or third left interspaces In one quarter of the cases with Eisen menger s complex proper however the murmur was loudest lower down

in the third and fourth spaces and may have been due to turbulence set up at the defect In two such instances the phonocardiogram showed it to be pansystolic A thrill accompanied the systolic murmur in one sixth of those with A S D one half of those with V S D and one quarter of those with patent ductus

The *second heart sound* was single or closely split (0 01 to 0 02 sec) with equal frequency in three quarters of the cases with V S D and obviously split (0 03 to 0 05 sec) in the remainder with patent ductus it was usually closely split and very rarely single with A S D it was obviously or even widely split (0 07 sec) in nearly half the cases and never single The pulmonary element of the second sound was nearly always loud unless pulmonary incompetence was severe

A *Graham Steell murmur* due to functional pulmonary incompetence was heard in two thirds of all cases and was equally frequent in each group

Electrocardiogram

Auricular fibrillation occurred in only two instances in a woman of 65 with atrial septal defect and a man of 62 with ventricular septal defect

Complete heart block occurred in two cases both with V S D

The *P wave* was extra sharp and measured 2 mm or more in amplitude (average 2 75 mm) in the most favourable lead in 56 per cent of cases with A S D or V S D but was normal in all but three cases with patent ductus in these three exceptions it measured only 2 mm in amplitude

Considerable right ventricular preponderance (grade 3 or 4) in chest leads was seen in 70 per cent of those with atrial septal defect and in *37 per cent* of those with ventricular septal defect or patent ductus its frequency being much the same in the last two groups *Normally balanced QRS T complexes* were never seen when the shunt was at atrial level but occurred in *16 per* cent of those with V S D *Right bundle branch block* was seen occasionally in each group (total 8 per cent)

X ray appearances

Conspicuous dilatation of the pulmonary artery was almost invariable it averaged grade 3 in those with A S D grade 2 in those with V S D and something between the two but nearer grade 3 in those with patent ductus

A *clear gap* or obvious concave recess *between the aortic knuckle and pulmonary arc* was rarely seen in cases with patent ductus (fig 8 54) but was well defined in about a quarter of those with Eisenmenger s complex or atrial septal defect (fig 8 55) A calcified arc identifying a patent ductus was seen only once The aortic knuckle was usually inconspicuous in all three groups but perhaps less so in those with patent ductus a prominent aortic knuckle was only seen in older subjects and then did *not help to* determine the site of the shunt

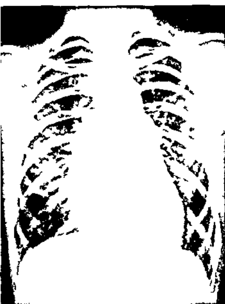


Fig 8 54—Case of pulmonary hypertension with reversed aorto pulmonary shunt through a patent ductus which can be seen as an abnormal convexity between the aortic knuckle and pulmonary arc



Fig 8 55—Case of pulmonary hypertension with reversed interatrial shunt showing a concave recess between the aortic knuckle and pulmonary arc

Dilatation of the right ventricle and atrium was most marked in cases with atrial septal defect and least evident in Eisenmenger s complex proper Thus in the former group grade 3 enlargement was recorded in two thirds of the cases whereas in the latter it was recorded in only 16 per cent Again the heart shadow was rarely normal in size when the shunt was interatrial whereas it was normal in 45 per cent of cases when the shunt was inter ventricular The average size of the heart shadow in cases with patent ductus lay midway between the two

The *peripheral pulmonary vascular markings* were light in nearly all cases (fig 8 56) in those with patent ductus or ventricular septal defect even the right main branch of the pulmonary artery was usually unimpressive only the left branch (left middle arc) being really conspicuous With atrial septal defect the proximal vessels tended to be heavier (fig 8 57)

A *right sided aortic arch* joining a right dorsal aorta occurred in 12 per cent of cases of Eisenmenger s complex proper (fig 8 58) but was never seen with A S D or patent ductus

Angiocardiography

In Eisenmenger s complex the ascending aorta and pulmonary artery opacify simultaneously from the right ventricle (fig 8 59) with atrial septal defect diaginol enters both atria and both ventricles more or less

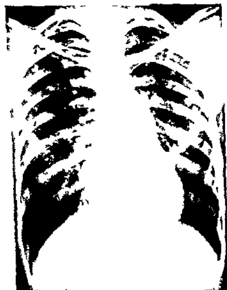


Fig 8 56—Eisenmenger s complex proper showing dilatation of th pulmonary artery and sl ght pulmonary ischæmia

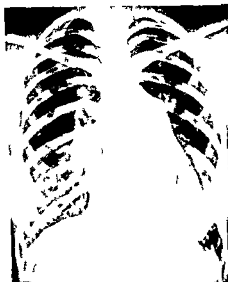


Fig 8 57—Eisenmenger s syndrome asso ciated with atrial septal defect showing considerable enlargement of the heart and dilatation of the prox mal branches of both pulmonary arteries the peripheral vascular shadows however are narrow

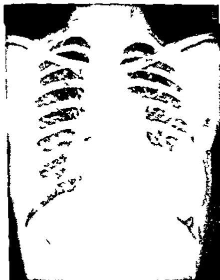


Fig 8 58—R ght s d d dorsal orta and dilatat on of the pulmon y artery in a cas of Eisenm nger s complex proper

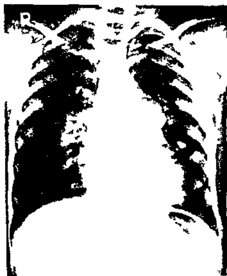


(a) Anterior view



(b) Second oblique position

Fig 8 59—Angiocardiogram in a case of Eisenmenger s complex proper showing simultaneous filling of the whole of the aorta and pulmonary artery mainly from the right ventricle although diaginol has also entered the left ventricle



(a) Anterior skiagram



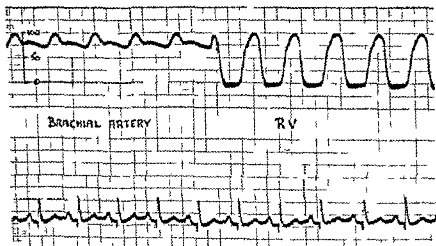
(b) Angiocardiogram showing opacification of the right side of the heart pulmonary artery and descending aorta the ascending aorta remaining translucent

Fig 8 60—Case of Eisenmenger s syndrome associated with patent ductus

simultaneously becoming much diluted in the process so that good contrast is more difficult to obtain with patent ductus the opaque medium enters the descending aorta from the pulmonary artery (fig 8 60)

Dye concentration curves

Evans blue dye injected selectively into the right ventricle through a cardiac catheter appears in the ear immediately in cases of Eisenmenger's complex its concentration being strongly fortified a few seconds later by dye that has passed through the lungs With atrial septal defect the initial hump is only seen when dye is injected into the right atrium and with patent ductus it is not seen at all in the majority of cases for little if any



Pap r p d 25 mm s c

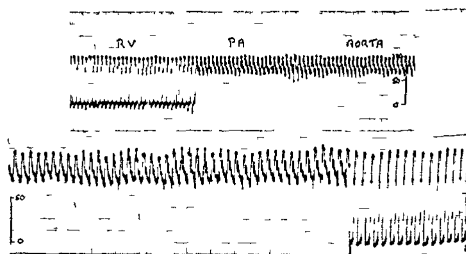
Fig 8 61—Immediately consecutive pressure tracing from th[illegible] and right ventricle in a case of Eisenmenger's complex p p

shunted dye enters the carotids on the other hand dye injected directly into the pulmonary artery appears at once in samples obtained from the femoral artery

Cardiac catheterisation usually reveals a *bidirectional shunt* at atrial ventricular or pulmonary artery level according to the site of the communication between the two circulations as pointed out by Bing *et al* (1947) In the present series the shunt was bidirectional in half the cases with atrial septal defect three quarters of the cases with ventricular septal defect and one third of the cases with patent ductus In three cases with patent ductus (18 per cent) there was *no shunt either way* but the catheter was passed through the duct and the systemic and pulmonary artery pressures were identical A perfectly balanced state of this kind was never

encountered with atrial or ventricular septal defect In the remainder of each group the *shunt was wholly reversed* The magnitude of the shunt was rarely great either way being usually of the order of 2–3 litres per minute The pulmonary blood flow averaged around 4 5 litres per minute in all groups With bidirectional shunts there was often very little difference between net systemic and net pulmonary blood flows but unidirectional reversed shunts naturally resulted in reduction of the pulmonary flow, which in such cases averaged 3 3 litres per minute

The *systolic pressure* in the two circulations was identical in all cases of Eisenmenger s complex (fig 8 61) and in all but one with patent ductus



Paper sp ed 5 mm sec

Fig 8 62—Immediately consecutive pressure tracings from the descending aorta and pulmonary artery in a case of Eisenmenger s syndrome associated with patent ductus

(fig 8 62) the *diastolic pressure* was also identical in nearly half these cases but when there was a difference the aortic diastolic pressure was usually higher than the pulmonary in Eisenmenger s complex and lower with patent ductus With atrial septal defect the systolic pressures in the two circulations were much closer than expected commonly within 5 mm Hg of each other the diastolic however was usually higher on the systemic side sometimes considerably so

The *pulmonary vascular resistance* averaged around 17 units in all groups the common range being between 13 and 22 units

In cases with patent ductus no difficulty was ever experienced in passing the catheter through it from the pulmonary artery to the descending aorta (fig 8 63) failure to do so under technically favourable conditions making the diagnosis virtually untenable In Eisenmenger s complex the ascending aorta was entered from the right ventricle in 40 per cent of cases, and with





(a) Anterior view (b) Second oblique position

Fig 8 63—Case of Eisenmenger's syndrome showing the usual lie of a catheter when it passes down a patent ductus into the descending aorta





Fig 8 64—Case of Eisenmenger syndrome associated with atrial septal defect the catheter has passed through the defect and is lying in (a) the left upper pulmonary vein and (b) the left lower pulmonary vein

happened Clinically the physical signs were those of simple atrial septal defect apart from the cyanosis clubbing and polycythæmia

A somewhat similar situation arises in *cases having a common atrium* and in advanced atrial septal defect with right ventricular failure or tricuspid incompetence although reversal of the shunt does not occur at all readily in this latter group At the bedside the tell-tale signs of pulmonary hypertension are missing With a common atrium blood samples from all chambers and from both systemic and pulmonary arteries are similar Since the right ventricle offers less resistance to filling than the left the pulmonary blood flow is increased as in simple atrial septal defect unless the pulmonary vascular resistance is high

Total anomalous pulmonary venous drainage into the right atrium also suggests atrial septal defect with reversed shunt but without pulmonary hypertension This is discussed fully later

2 *Transposition of the great vessels with patent septa* If there is a high pulmonary vascular resistance the physiological situation is very like Eisenmenger s complex a bidirectional shunt taking place at ventricular level and the systolic pressure in the two circulations being identical but pulmonary artery samples are more saturated with oxygen than aortic samples since the former derive chiefly from the left ventricle and the latter from the right

Persistent truncus arteriosus with the pulmonary arteries arising from the root of the aorta is physiologically like Eisenmenger s complex only when the pulmonary vascular resistance is high Radiologically the aortic root is unduly prominent however and although the left branch of the pulmonary artery may be conspicuous the main pulmonary trunk is absent The diagnosis may be proved by angiocardiography or cardiac catheterisation as described later



Fig 8 65—Skiagram of a case of anoxic cor pulmonale due to emphysema complicating atrial septal defect with direct left to right shunt

3 *Primary pulmonary hypertension* with late reduction of arterial oxygen saturation to around 80 per cent may be distinguished by its relatively short duration (usually less than two years) rapid development of heart failure marked peripheral cyanosis giant *a* waves in the jugular pulse right atrial gallop frequent absence of a pulmonary systolic murmur

tall P pulmonale and gross right ventricular preponderance electrocardiographically angiocardiography shows no right to left shunt and cardiac catheterisation no left to right shunt the pulmonary artery pressure is usually lower than the systemic at rest and higher on effort

4 *Anoxic cor pulmonale* with secondary pulmonary hypertension and a normal or reduced cardiac output can usually be recognised by the history and the presence of advanced emphysema When the causal bronchitis and emphysema complicate atrial septal defect bedside diagnosis can be very difficult (fig 8 65) Catheterisation however then reveals a unidirectional shunt from left to right atrium and pulmonary venous samples as unsaturated as those from the left atrium left ventricle and systemic arteries as in the case illustrated which was later confirmed at necropsy

PROGNOSIS

Of 35 fatal cases of Eisenmenger s complex reported in the literature and reviewed by Selzer and Laqueur (1951) 8 died in infancy 4 between the ages of three and ten and 5 7 7 1 and 3 in each subsequent decade respectively the oldest being 60 Figures for pulmonary hypertension with reversed interatrial or aorto pulmonary shunt should not be dissimilar and since ages are always younger in necropsy series it follows that on the whole the prognosis is fair The ages of the patients in the present series (tabulated earlier) confirm this view

TREATMENT

Surgical repair of the defect is contra indicated in all forms of the Eisenmenger syndrome because it not only fails to relieve the pulmonary hypertension but also removes the safety valve in the pulmonary circulation It must be clearly understood however that pulmonary hypertension due to a raised pulmonary vascular resistance is no bar to ligation of a patent ductus or repair of an atrial septal defect if the pulmonary blood flow is still elevated i e if the left to right shunt is still dominant for the resistance may be expected to fall if the pulmonary blood flow can be reduced to normal *Surgical correction of central cyanosis is not the therapeutic objective in Eisenmenger s syndrome and if performed can only be regarded as a cosmetic operation which endangers life*

PULMONARY STENOSIS

CLASSIFICATION AND FREQUENCY

ACYANOTIC		CYANOTIC	
Normal aortic root		*Dextroposed aortic root*	
Simple (with closed septa)		Fallot s tetralogy	
valvular		chiefly valvular	4%
infundibular		chiefly infundibular	7%

With direct left to right shunt via		(pulmonary atresia 1 7%)	
		Normal aortic root	
patent ductus	rare	Pulmonary stenosis with reversed shunt	
V S D	1 3%	interventricular	rare
A S D	2%	interatrial	3%

Anatomically and embryologically the fundamental difference between the two main types of pulmonary stenosis depends on the position of the aortic root in simple stenosis whether the septa are patent or not the aortic root is normal and arises wholly from the left ventricle posteriorly and to the left in Fallot s tetralogy it is dextroposed and arises partly from the right ventricle so that it sits astride the interventricular septum which is necessarily defective In the former the pulmonary artery completely covers the root of the aorta crossing over it anteriorly from right to left in the latter the root of the pulmonary artery is displaced to the left and posteriorly so that it may not cover the aorta at all the origins of the two vessels tending to lie side by side the aorta on the right the pulmonary artery on the left

In simple stenosis the stricture is valvular in 80 per cent and infundibular in 20 per cent in Fallot s tetralogy it is mainly valvular in 40 per cent and mainly infundibular in 60 per cent In valve stenosis the cusps are fused or represented by a conical membrane with a small circular hole in the centre In fundibular stenosis a small chamber the primitive bulbus cordis (Keith 1909) is separated off from the body of the right ventricle by a fibrous ring which is the seat of the obstruction

Physiologically Fallot s tetralogy is pulmonary stenosis with reversed interventricular shunt and the only difference between it and simple pulmonary stenosis with ventricular septal defect is the degree of stricture which is sufficient to reverse the shunt in the former and usually insufficient to do so in the latter In relatively mild cases of Fallot s tetralogy and in severe cases after infundibular resection the shunt may be wholly from left to right despite the over riding aorta again in simple stenosis with ventricular septal defect the shunt may be reversed if the stricture is tight enough

PULMONARY STENOSIS WITH NORMAL AORTIC ROOT

INCIDENCE

Of all cases of congenital heart disease only atrial septal defect (18 per cent) is more common than pulmonary stenosis with normal aortic root (16 per cent excluding cases in which associated atrial septal defect or ventricular septal defect is dominant)

The sex ratio was unity in the series analysed here

The age distribution was as follows

Age	0–10	11–20	21–30	31–40	41–70
No per cent	38	35	19	5	3

It was more or less similar in all sub groups The oldest patient in the series was 67

HAEMODYNAMICS

Pulmonary stenosis obviously interferes with the free passage of blood to the lungs and to overcome the obstruction the right ventricle must contract more powerfully This is achieved by hypertrophy and increased diastolic stretch The right atrium helps by contracting more strongly and forcibly distending the right ventricle at the end of diastole (fig 2 22) A giant *a* wave in the jugular pulse right atrial gallop and a tall P pulmonale are manifestations of this atrial contribution

In mild cases normal pulmonary artery pressures and flows are easily maintained with right ventricular systolic pressures of only 25 to 50 mm Hg (at rest) When the stricture is moderate satisfactory pulmonary artery pressures and flows can still be maintained with right ventricular systolic pressures of 50 to 100 mm Hg In severe cases, however the cardiac output is low and fixed and the pressure in the pulmonary artery is low despite systolic pressures in the right ventricle between 100 and 300 mm Hg Peripheral vasoconstriction helps to maintain the systemic blood pressure

In these severe cases the resistance of the stenosis is greater than the peripheral systemic resistance so that the right ventricular systolic pressure is higher than the left If there is an associated ventricular septal defect the ventricular pressures are equalised as in Fallot s tetralogy by a shunt flow from right to left Without such a safety valve right ventricular pressures may rise very high indeed and the right atrial pressure also owing to the resistance of the thick right ventricle to extra diastolic stretch If the foramen ovale is patent or if there is an associated atrial septal defect shunt reversal then takes place at atrial level thereby relieving the right ventricle of some of its load

In cases of mild or moderate severity pressures in the right side of the heart are lower than in the left and an associated ventricular septal defect or atrial septal defect results in the usual direct left to right shunt

CLINICAL FEATURES

In view of the physiological situation described above it is clear that the clinical behaviour of cases of pulmonary stenosis must vary greatly according to the severity of the lesion In the present series of 170 cases the stenosis was mild in 38 per cent moderate in 25 per cent and severe in 37 per cent These three groups will be discussed first separately

Mild uncomplicated cases

There are no symptoms and effort tolerance is normal All cases are acyanotic

The only abnormal physical sign is a loud pulmonary systolic murmur usually initiated by a pulmonary ejection click (Leatham and Vogelpoel 1954) and accompanied by a thrill in 86 per cent There is no significant *a* wave in the venous pulse the cardiac impulse is normal (left ventricular) there is no lift over the right ventricle and the second heart sound is obviously split with the pulmonary element quite loud and clear

The electrocardiogram is normal Skiagrams show characteristic post stenotic dilatation of the pulmonary artery but nothing else abnormal

Uncomplicated cases of moderate severity

There are still no symptoms and all cases are acyanotic Effort tolerance is usually normal Included amongst the 80 patients with uncomplicated pulmonary valve or infundibular stenosis of mild or moderate grade were a New Zealand long distance swimming champion a woman athlete a Cambridge University wing three quarter a captain of a regional English hockey XI and a first class long distance runner

In addition to the thrill and murmur the physical signs now include slight exaggeration of the jugular *a* wave (about 3 mm Hg) an impalpable left ventricle and wide splitting of the second heart sound the pulmonary component being late none too loud, curiously brief and rather high pitched even metallic in quality

The electrocardiogram always shows some degree of right ventricular preponderance usually grade 2 sometimes grade 1 or grade 3 but never grade 4 A small P pulmonale (2 mm /0 08 sec) is seen in about 40 per cent of cases

Fluoroscopy still reveals no more than post stenotic dilatation of the pulmonary artery in one third of the cases (fig 8 66) but in two thirds there is now slight enlargement of the right side of the heart and occasionally (15 per cent) slight pulmonary ischæmia



Fig 8 66—Skiagram of a case of simple pulmonary valve stenosis showing post stenotic dilatation of the pulmonary artery

Uncomplicated severe cases

When the stricture is severe *effort dyspnœa* ranges between none (10 per cent) slight (30 per cent) moderate (30 per cent) and considerable or gross (30 per cent together) *Angina pectoris* occurred in 15 per cent of the 32 uncomplicated cases in the present series and *syncope* in 12 per cent

The physical signs are highly characteristic and usually pathognomonic The face is highly coloured unusually full even bloated (moon facies) in one third of the cases not unlike that in patients treated with A C T H (fig 8 67) Cyanosis when present is peripheral unless the foramen ovale is patent (*vide infra*) The pulse is usually small and the blood pressure normal or rather low



Fig 8 67—The moon facies in a case of pulmonary valve stenosis

There was a *giant a wave* (fig 8 68) in the jugular venous pulse reaching 5 to 15 mm Hg above the sternal angle in half the severe cases and a smaller but clearly dominant *a* wave measuring about 3 mm Hg in a quarter Of the remainder some had a normal venous pulse and a similar number had gross tricuspid incompetence The giant *a* wave is of course presystolic in timing peculiarly abrupt and collapsing in quality (like a venous Corrigan s sign) can be felt as well as seen and is transmitted to the liver it leaps to the eye towering above and dwarfing the other waves of the venous pulse (Abrahams and Wood 1951)

The left ventricle is always impalpable in severe cases but a conspicuous *right ventricular heave* may be seen and felt from the left sternal edge to the mid clavicular line or beyond, this parasternal lift should be felt as high as the third space provided the stenosis is valvular

Right atrial presystolic gallop usually accompanies the giant *a* wave A pulmonary ejection click does not occur in severe cases (Leatham and Vogelpoel 1954) A loud and long *pulmonary systolic murmur*, invariably accompanied by a thrill spills through the aortic second sound and the *pulmonary second sound* is either inaudible or both very late and very quiet With only two exceptions the murmur was heard best in the second left space in all these cases of valve stenosis

The *electrocardiogram* invariably shows considerable or gross right ventricular preponderance (fig 8 69) apart from rare instances in which

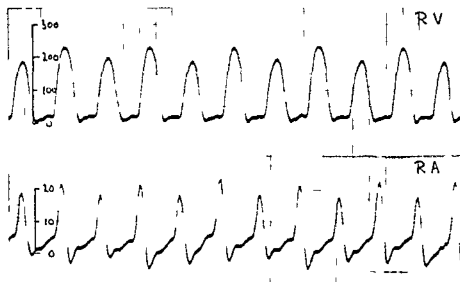


Fig 8 68—Giant *a* wave measuring 20 mm Hg in a case of severe pulmonary valve stenosis note the alternation in both right atrial and ventricular pressures

there is fully developed right bundle branch block A tall P pulmonale averaging 3 mm nearly always accompanies the QRS T changes

Skiagrams show a small aorta post stenotic dilatation of the pulmonary artery light pulmonary vascular markings and a variable degree of right atrial and ventricular enlargement (fig 8 70) occasionally the latter is so gross that it masks the dilated pulmonary artery

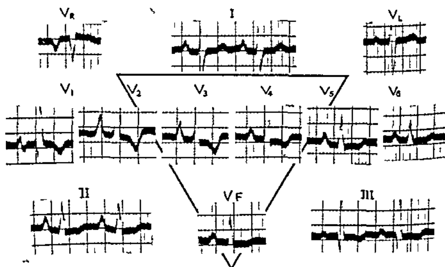


Fig 8 69—Gross right ventricular preponderance in a case of severe pulmonary stenosis (infundibular)



Fig 8 70—Severe pulmonary valve stenosis showing a small aorta conspicuous dilatation of the pulmonary artery pulmonary ischæmia and considerable dilatation of the right side of the heart

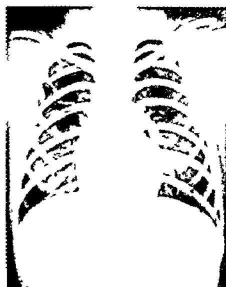


Fig 8 71—Infundibular stenosis showing no dilatation of the pulmonary artery

INFUNDIBULAR STENOSIS

Simple infundibular stenosis whether mild moderate or severe differs from the type described above in three respects only (1) no right ventricular lift may be felt as high as the third left space (2) the thrill and murmur are usually maximum low down in the fourth space or even at the apex (3) there is rarely radiological evidence of post stenotic dilatation of the pulmonary artery (fig 8 71) Unfortunately there are exceptions to all these rules but the first is true in over half the cases the second in 80 per cent and the third in 85 per cent When mild or moderate infundibular stenosis is usually mistaken for maladie de Roger

PULMONARY STENOSIS WITH DIRECT SHUNT

When an atrial or ventricular septal defect complicates pulmonary stenosis with normal aortic root the shunt is direct from left to right if the stricture offers less resistance to flow than the systemic peripheral resistance The clinical features vary according to the degree of stricture and the size of the defect and are determined chiefly by the dominant lesion

When atrial septal defect is dominant pulmonary stenosis should be suspected if there is a pulmonary ejection click a coarse systolic thrill and

unusually wide splitting of the second heart sound When ventricular septal defect is dominant the stenosis is usually overlooked When pulmonary valve or infundibular stenosis is dominant relatively small direct shunts are apt to escape notice but may be suggested by discrepancy between the size of the right ventricle and the pulmonary vascular shadows

PULMONARY STENOSIS WITH REVERSED INTERATRIAL OR INTERVENTRICULAR SHUNT

Moderately severe cases of pulmonary stenosis may have a patent foramen ovale that is functionally closed As life advances, the stricture may tighten the pressure in the right side of the heart then rises and the foramen ovale may suddenly begin to function and permit the passage of blood from right to left atrium Such cases illustrate very well what is meant by late central cyanosis or cyanose tardive. Patients with pulmonary stenosis and A S D or V S D may behave similarly

The change is apt to occur in adolescence and is accompanied by the development of breathlessness (Allanby and Campbell 1949) Cyanosis is notably variable and patients may only turn blue on exertion Pulmonary stenosis with reversed interventricular shunt resembles Fallot s tetralogy, but the aorta is not over riding

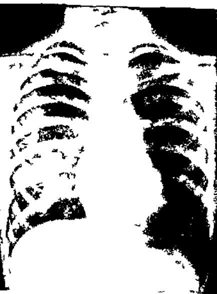
In most severe cases of pulmonary stenosis however the pressure in the right atrium exceeds that in the left from birth and the foramen ovale cannot close Under these circumstances patients have permanent central cyanosis and proportionate functional incapacity from birth In the present series of 30 cases with reversed interatrial shunt breathlessness and cyanosis had been present since birth in 80 per cent cyanosis had appeared first between the ages of 8 and 16 in 12 per cent and the remainder were clinically acyanotic at rest According to Joly *et al* (1950) the condition was described by Fallot in 1888 and has therefore been called Fallot s trilogy by the French school

The clinical features are similar to those of severe pulmonary stenosis with closed septa with the addition of *central cyanosis clubbing* and *polycythaemia*, together with certain other modifications *Effort intolerance* usually dating from birth is moderate or considerable with equal frequency in the vast majority occasionally it is gross (and of course must become so in the end) but it is very rarely slight Since the right ventricle is spared some of the load and therefore fares better than cases of equal severity without a defect in the atrial septum (Brecher and Opdyke 1951) the greater effort intolerance must be due to the drop in arterial oxygen saturation as it is in Fallot s tetralogy Both angina pectoris and syncope occurred only twice each in the 30 cases comprising this series

A *moon facies* was seen in a quarter of the cases *arachnodactyly* in 11 per cent and hypertelorism in two instances A *giant a wave* 5 to 55 mm Hg in amplitude was recorded in 60 per cent and a dominant *a*

3 mm Hg above *v* in 26 per cent Two of the cases with giant *a* waves that came to necropsy had large atrial septal defect, so that powerful right atrial contraction does not necessarily mean a small foramen ovale A *right ventricular heave* was slight (or even absent) in half the cases moderate in a quarter and considerable in a quarter

The characteristic *thrill and long murmur* and their lower position when the stenosis was infundibular were the same as in acyanotic cases The thrill was absent in only two instances The *second heart sound* was single (aortic) in all but three cases and in these it was very late A very soft late P could often be demonstrated however phonocardiographically In three instances a soft relatively short mid diastolic murmur could be heard in the third left space and was attributed to turbulence set up at the atrial septal defect in two others there was a murmur strongly suggesting slight pulmonary incompetence



(a) Showing dilatation of the pulmonary arc and pulmonary ischæmia



(b) Showing considerable cardiac enlargement and pulmonary ischæmia

Fig 8 72—Pulmonary stenosis with reversed interatrial shunt

Teleradiograms showed considerable dilatation of the right heart in only a quarter of the cases moderate enlargement being the rule and slight or no enlargement occurring in one third (fig 8 72) There was usually more pulmonary ischæmia than in acyanotic cases Post stenotic dilatation of the pulmonary artery was seen in nearly all those with valve stenosis

The *electrocardiogram* showed evidence of considerable or gross right atrial and right ventricular hypertrophy in 85 per cent

DIFFERENTIAL DIAGNOSIS

Mild pulmonary stenosis may be confused with atrial or ventricular septal defect idiopathic dilatation of the pulmonary artery mild aortic stenosis and normality *Atrial septal defect* should be distinguished by the size and behaviour of the right ventricle the absence of a pulmonary ejection click fixed splitting of the second sound frequent mid diastolic murmur associated with tricuspid turbulence partial right branch block pattern of the electrocardiogram and pulmonary plethora

Maladie de Roger is easily confused with mild infundibular stenosis, but may be suggested by the closer splitting of the second heart sound Maladie de Roger should not be mistaken for mild pulmonary valve stenosis in view of the earlier and lower position of the systolic murmur absence of a pulmonary ejection click closer splitting of the second sound and absence of dilatation of the pulmonary artery The clinical features of pulmonary stenosis and ventricular septal defect diverge more and more widely as their severity increases

Idiopathic dilatation of the pulmonary artery may give rise to difficulty when the pulmonary ejection click is followed by a grade 2 systolic murmur In fact in such cases it is often impossible to be sure whether there is trivial stenosis or not and one may be still in doubt when cardiac catheterisation reveals a 5 to 10 mm Hg pressure gradient across the pulmonary valve when the right ventricular systolic pressure is still within normal limits

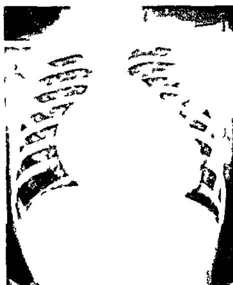


Fig 8 73—Pulmonary valve stenosis with gross dilatation of the right ventricle and atrium resulting in appearances similar to those of Ebstein s disease except for the dilatation of the pulmonary artery

In *mild aortic stenosis* the systolic murmur and thrill begin later and end well before the second heart sound which is closely split A being slightly delayed moreover the murmur is well heard at the apex beat and over the right carotid

A *normal heart* with a grade 2 functional pulmonary ejection *murmur and prominence* of the pulmonary arc radiologically may also be mistaken for mild stenosis

Pulmonary stenosis of moderate severity is one of the easiest bed side diagnoses and can hardly be mistaken for anything else whether the stricture is valvular or infundibular

Severe stenosis is also unmistakable in acyanotic cases unless there is gross failure In such instances a deep y descent or large systolic wave

from tricuspid incompetence may replace the giant *a* of the jugular pulse the overloaded and grossly distended right heart loses its former vigour and may not be recognised by palpation the electrocardiogram may show right bundle branch block, and X rays reveal a grossly enlarged stencilled heart shadow (fig 8 73) which in view of the findings just mentioned i easily mistaken for that of Ebstein s disease However the typical thrill and murmur of stenosis are still present and the characteristic diastolic scratch of Ebstein s disease is missing moreover it is very rare to meet the full combination of confusing features described above and as a rule a giant *a* wave right ventricular heave high voltage electrocardiogram with gross right ventricular preponderance or post stenotic dilatation of the pulmonary artery makes a diagnosis of Ebstein s disease untenable

Severe stenosis with reversed shunt may be confused with *Fallot s tetralogy* Favouring a normal aortic root and atrial septal defect are arachnodactyly a moon facie giant *a* wave considerable right ventricular heave right atrial gallop long systolic murmur and thrill faintly audible late P soft mid diastolic murmur in the third or fourth left space gross right ventricular preponderance electrocardiographically considerable enlargement of the right heart radiologically and post stenotic dilatation of the pulmonary artery for all these features are absent in Fallot's tetralogy

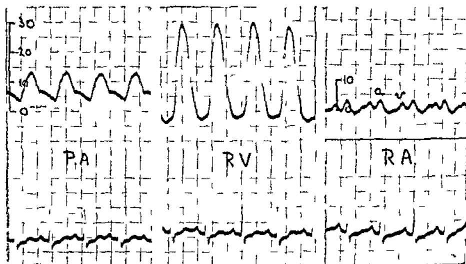
A history of squatting normal venous pressure and pulse quiet heart short systolic thrill and murmur loud single (aortic) second sound moderate right ventricular preponderance electrocardiographically normal transverse diameter of the heart radiologically a poorly defined pulmonary arc and a right sided thoracic aorta all favour Fallot s tetralogy

PHYSIOLOGICAL FINDINGS (based on 150 cases catheterised)

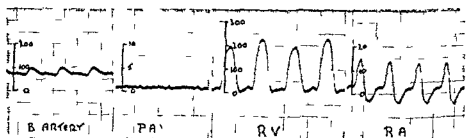
In *mild cases* of pulmonary stenosis with normal aortic root the right atrial pressure is normal the right ventricular pressure 30/0 to 50/0 and the pulmonary artery pressure normal (fig 8 74a) the cardiac output is normal and rises normally with effort with the aid of some elevation in right ventricular pressure The arterial oxygen saturation is normal

In *moderate cases* the findings are similar except that a dominant *a* wave measuring about 3 mm Hg may appear in the right atrial tracing and the right ventricular systolic pressure lies between 50 and 100 mm Hg at rest and may rise well over 100 on effort

In *severe cases* a giant *a* wave rising 5 to 15 mm Hg above the zero point is almost invariable The right ventricular pressure lies between 100/0 and 275/20 at rest the raised end diastolic pressure being usually due to the giant *a* rather than to heart failure The pulmonary artery pressure is usually low (fig 8 74b) The right ventricular systolic pressure is commonly higher than the systemic blood pressure at rest and rises well above it on exercise The cardiac output is low and rises little on exertion the arterio-venous oxygen difference is nearly always over 50 ml per litre and



(a) Mild



(b) Severe

Fig 8 74—Pressure tracings from two cases of pulmonary valve stenosis

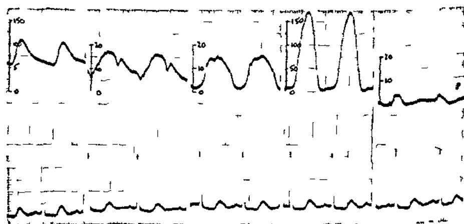


Fig 8 75—Pressure tracings from a case of infundibular stenosis The systolic pressure in the infundibular chamber is the same as that in the pulmonary artery while the diastolic pressure is the same as that in the right ventricle

increases greatly on effort The arterial oxygen saturation is normal in cases with closed septa

When the stenosis is infundibular the systolic pressure in the infundibular chamber is the same as that in the pulmonary artery while the diastolic pressure is the same as that in the right ventricle (fig 8 75) The position of the tip of the catheter when the systolic pressure changes provides good evidence concerning the site of the stricture

Pulmonary stenosis with atrial septal defect or ventricular septal defect and direct left to right shunt is proved by finding an increased oxygen saturation in samples taken from the right atrium or right ventricle respectively in addition to a significant systolic pressure gradient across the pulmonary valve or infundibulum

In severe pulmonary stenosis with reversed interatrial shunt it is usually possible to pass the catheter through the defect into the left atrium and left ventricle or out into a pulmonary vein (fig 8 76) In the 30 cases catheterised the right ventricular systolic pressure ranged between 105 and 260 averaging 165 mm Hg and was usually well above the left ventricular pressure (fig 8 77) Giant *a* waves in right atrial pressure tracings were never transmitted to the left atrium in cases with relatively small shunts due to patent foramen ovale (fig 8 77) but were seen occasionally in left atrial tracings when the shunt was large and due to atrial septal defect proper The arterial oxygen saturation averaged 75 per cent and arterial samples were similar to those obtained from the left ventricle but left atrial samples varied considerably according to whether the tip of the catheter was lying in the shunt stream or near the mouth of a pulmonary vein Pulmonary venous samples were always normally saturated

In the differential diagnosis between pulmonary stenosis with reversed interatrial shunt and Fallot s tetralogy there are two points of crucial importance (1) a catheter may pass through a valve patent foramen ovale in Fallot s tetralogy but when it does so left atrial samples are usually fully saturated the foramen being functionless (2) when the right ventricular systolic pressure is more or less the same as the systemic blood pressure simultaneous or immediately consecutive right ventricular and brachial arterial pressures should be recorded both at rest and on exercise for in Fallot s tetralogy they remain identical whereas in pulmonary stenosis with reversed interatrial shunt they do not Slight differences between right ventricular and systemic arterial pressures at rest may be due to artefact or over damping in one of the systems or to a slight local build up of pressure in the femoral artery if that vessel is used and do not therefore exclude Fallot s tetralogy

Selective dye concentration curves may prove the site of a reversed shunt If Evans blue dye is injected into the right ventricle for example it appears immediately in the ear only when the shunt is at ventricular or aorto pulmonary level



(a) (b)



(c) (d)

Fig 8 76—Pulmonary stenosis with reversed interatrial shunt the catheter has passed through the defect and is lying (a) in the right upper pulmonary vein (b) in the right lower pulmonary vein (c) in the left upper pulmonary vein and (d) in the left atrium close to the mitral valve

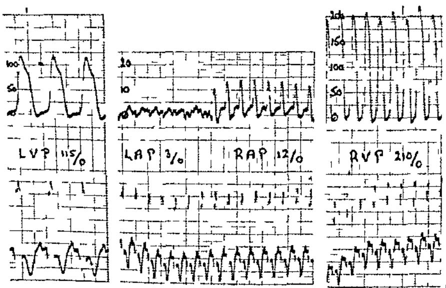


Fig 8 77—Pressure trac ngs from a case of pulmonary al e stenosis ith reversed interatrial shunt showing giant *a* waves in the right atrium but not in the left

ANGIOCARDIOGRAM

Routine intravenous angiocardiograms demonstrate the site of pul monary stenosis in the majority of cases but by no means in all selective angiocardiograms obtained after injecting diaginol into the right ventricle preferably through a wide catheter pro vided with lateral holes near the tip so as to avoid recoil are more informative (Jons son Broden and Karnell 1953) Whether the stricture can be seen directly or not angiocardiography may con firm the diagnosis of pulmon ary stenosis in three indirect ways (1) there is a hold up in the passage of the contrast medium through the right side of the heart which is proportional to the severity of the stricture (2) during systole in cases of valve stenosis powerful contraction



F g 8 78—Ang oca d ogram in a case of pulmonary stenosis ith r versed intra at l shunt the con tra t medium i pass ng through both s des of the heart multaneously

of the hypertrophied infundibulum may cause remarkable narrowing of the outflow tract (3) post stenotic dilatation of the pulmonary artery is well demonstrated in cases of valve stenosis

In cases with reversed interatrial shunt there is more or less simultaneous filling of both sides of the heart (fig 8 78) With selective angiocardiography simultaneous filling of the aorta and pulmonary artery is only seen when diaginol is injected into the right atrium

COURSE AND PROGNOSIS

The average age of death in cases that have come to necropsy was 20 6 years in Abbott s (1931) series 22 8 years in the group reported by Bauer and Astbury (1944) and 26 in the series reviewed by Green *et al* (1949) The usual cause of death was congestive heart failure which was three times as common as bacterial endocarditis It follows that these serious mortality figures apply chiefly to severe cases for mild stenosis does not cause heart failure and moderate stenosis is unlikely to do so

The oldest case in Green s series was 75 years the oldest in my own 67 This was a man still in fairly good health apart from emphysema the clinical features fulfilled the criteria for mild or moderate stenosis partly masked by emphysema his right ventricular pressure was 75/3 pulmonary artery pressure 15/3 and right atrial pressure 3 —3 0 —3 for *a x v* and y respectively, the cardiac output at the time being 3 7 litres per minute the right ventricle was not dilated radiologically and there were no signs of impending break down There can be little doubt therefore that the prognosis of mild and moderate cases is good apart from the risk of bacterial endocarditis

Severe cases whether acyanotic or with reversed shunt, become progressively incapacitated but may linger on with chronic congestive failure and ascites The oldest acyanotic case in this group was 33 when he died the oldest with central cyanosis 26 years

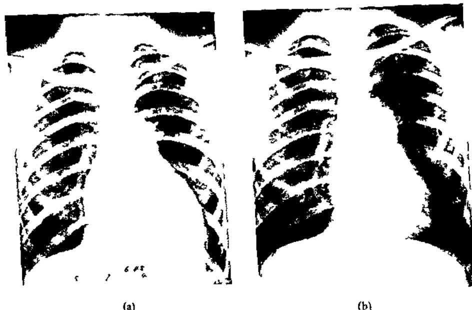
Bacterial endocarditis has not yet been witnessed in any case in the present series but two of the patients gave a convincing history of it Prior to the infection both had had grade 3 effort intolerance one of them having had considerable central cyanosis obviously due to reversed interatrial shunt Following cure of the infection both improved remarkably, one being now symptom free the other having only slight effort intolerance These are the only two cases in the whole series with obvious pulmonary diastolic murmurs and it seems reasonable to conclude that the infection performed a medical valvotomy

Pulmonary tuberculosis complicated two severe cases one of them acyanotic the other with reversed shunt it was met in only one other instance in this series despite the fact that one of the clinics at which patients were seen was at the Brompton hospital This gives an incidence of about 2 per cent which is the same as in the general population

TREATMENT

Mild cases should be encouraged to lead a normal life without any restrictions Cases of moderate severity do not require surgical help and should also be allowed to lead normal lives although competitive effort is probably best avoided Patients in all groups should be protected against dental and other sources of infection by means of penicillin or other suitable antibiotics when the occasion arises

Pulmonary valvotomy (Brock 1948 Brock and Campbell 1950) should be undertaken in all severe cases, preferably around the age of 6 to 10 Infundibular resection is better performed under direct vision either with



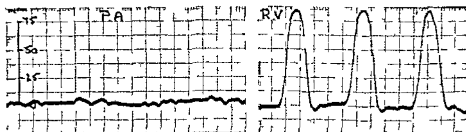
(a) (b)

Fig 8 79—Case of pulmonary valve stenosis (a) before and (b) after valvotomy showing considerable reduction in heart s ze following the operation

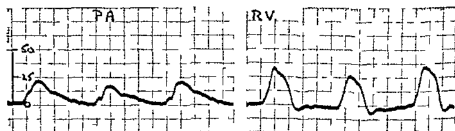
the help of hypothermia or crossed circulation Anastomotic operations are contraindicated in cyanotic cases because the increased pulmonary blood flow that results raises the left atrial pressure and by reducing the reversed shunt increases the load on the right ventricle which frequently fails Secondary elevation of the right atrial pressure then restores the right to left interatrial shunt so that little is gained at considerable cost

Pulmonary valvotomy was undertaken by Sir Russell Brock in 30 patients in this series and infundibular resection in four others The results were excellent or good in a little over half and fair or poor in a quarter 20 per cent died When the result was excellent patients became symptom free and cases with previously reversed shunt lost all trace of

cyanosis and clubbing The right ventricle and atrium diminished considerably in size (fig 8 79) and the electrocardiogram showed less right ventricular preponderance At operation effective valvotomy was considered to have been achieved when the pulmonary artery pressure rose to normal and developed a good pulse pressure while the right ventricular systolic pressure fell to 50 mm Hg or less (fig 8 80)



(a)



(b)

Fig 8 80—Case of severe pulmonary valve stenosis showing pulmonary artery and right ventricular pressure pulse (a) before and (b) after pulmonary valvotomy

At the present time the operative mortality is nearer 6 than 20 per cent (Campbell and Brock 1955) and the results from infundibular resection under direct vision are as good as those for valvotomy apart from the added risk of hypothermia

Pulmonary incompetence has never caused trouble in this group although a faint or moderate pulmonary diastolic murmur has been heard following valvotomy in nearly half the cases

Subsequent cardiac catheterisation a year or two later in a limited number of these cases has revealed physiological findings in harmony with the clinical situation the right ventricular systolic pressure being under 50 mm Hg at rest and the pulmonary artery pressure pulse normal in the best of them

PULMONARY STENOSIS WITH DEXTROPOSED AORTIC ROOT

(FALLOT'S TETRALOGY)

The combination of pulmonary stenosis patent interventricular septum riding' aorta and enlargement of the right ventricle is known as Fallot's tetralogy (Fallot 1888) and accounts for 66 per cent of cases of congenital heart disease with clubbing of the fingers, polycythæmia and permanent central cyanosis The stenosis is purely infundibular in just over half the cases purely valvular in about a third and both infundibular and valvular in the remainder The defect in the ventricular septum measures 10 to 16 mm in diameter according to the size of the heart (Brinton and Campbell 1953) The pulmonary artery instead of being dilated as in simple pulmonary stenosis is remarkably small at least in cases with infundibular stenosis and may resemble a vein By riding aorta is meant displacement of the root of the aorta to the right (dextroposed aorta) so that it sits astride the septum and appears to arise as much from the right as from the left ventricle The association of these three malformations is no accident but depends upon the same embryological defect the fault lying with arrested evolution of the bulbus cordis with incomplete torsion. A right sided aortic arch is found in 20 to 25 per cent of cases (Taussig 1947) an association not found in cases with normal aortic root It occurred in 20 per cent of the present series of 100 cases A left sided superior vena cava (always with a right S V C as well) was demonstrated by means of cardiac catheterisation or angiocardiography in 20 per cent also conversely Fallot's tetralogy was present in just over 50 per cent of all cases in which a left S V C was recognised no other condition except perhaps Eisenmenger's complex proper having any special association with it

Hæmodynamics Aortic blood is arterio venous being composed of the full output of the left ventricle and part of that from the right The right ventricle competes with the left ventricle against the systemic peripheral resistance, which is less than that of the stricture The situation is met by hypertrophy of the right ventricle, the fourth constant finding in the tetralogy The deficient pulmonary circulation is occasionally improved by extensive development of the bronchial vascular system Polycythæmia helps to compensate for anoxæmia

The pressures in the left and right ventricle are always identical, and on effort the right ventricular systolic pressure cannot rise above aortic level The right ventricle accommodates itself to this situation from birth and is as thick or thicker than its fellow it is not distended and rarely fails for it can empty freely and quickly into the aorta if the obstruction increases Since left and right atrial pressures are also practically identical in Fallot's tetralogy (easily demonstrated when there is a patent foramen ovale) diastolic ventricular tone must also be much the same on the two

sides This explains why there is no detectable interatrial shunt when there is a patent foramen ovale or small atrial septal defect

Relatively mild cases occur in which the resistance of the stenosis is about the same as the systemic peripheral resistance there is then a bidirectional shunt as in Eisenmenger s complex, or there may be a perfectly balanced state between the two circulations with no detectable shunt either way such cases being acyanotic at rest If the stenosis is milder still a unidirectional left to right shunt can occur as it may also after successful valvotomy or infundibular resection About 10 per cent of all cases of Fallot s tetralogy behave in one of these ways and help to prove that the direction and magnitude of the shunt are determined a great deal more by the total resistances in the two circulations than by the degree of over ride

FREQUENCY AGE AND SEX

Fallot s tetralogy accounted for 11 per cent of the author s series of 900 cases of congenital heart disease The number per cent in each decade was as follows

Age group	0–10	11–20	21–30	31–40	41–50
No per cent	50	33	15	1	1

The average age was 12 years the oldest 42 The sex ratio was 7 4 in favour of males This contrasted with the 3 4 M F ratio in pulmonary stenosis with reversed interatrial shunt

CLINICAL FEATURES

Cyanosis polycythaemia and *clubbing* of the fingers may be absent in infants but develop in early childhood and tend to be progressive Central cyanosis means an arterial oxygen saturation below 85 per cent. Of the 100 cases in this series 15 per cent were acyanotic at rest as described by Wood Magidson and Wilson (1954) and had neither polycythæmia nor clubbing The arterial oxygen saturation ranged between 87 and 97 per cent in this group Polycythæmia was demonstrated in 82 per cent of cyanosed cases Growth may be stunted but mental development is usually normal The bloated facies of severe pulmonary stenosis with normal aortic root is not seen in the tetralogy The chief symptom is *breathlessness* and to obtain maximum comfort children often adopt a characteristic *squatting* posture (Taussig 1947) Squatting improves the arterial oxygen saturation (Lequime Callebaut and Denolin 1950) but the reason for this is not yet clear Effort intolerance is usually considerable (grade 3) and is rarely less than grade 2B even in acyanotic ca es It is attributed to a fall in arterial oxygen saturation on effort and perhaps to some disturbance of ventilation not yet fully understood it is not due to right ventricular strain and temporary overloading of that chamber for nothing of that sort occurs

Angina pectoris is extremely rare but *syncope* occurs in 20 per cent of cases especially in infancy and early childhood Attacks may be related to effort crying breath holding or some other transient disturbance but are often capricious and unexpected Theoretically anoxic syncope might be expected to result from any agent which lowered the systemic resistance sufficiently to cause a critical increase of right to left shunt as demonstrated by Hamilton Winslow and Hamilton (1950) in fact however the blood pressure has not fallen in any of four cases studied by the author, nor did a powerful pressor agent which raised the blood pressure from 100 to 150 mm Hg in an infant make any difference to the grossly reduced pulmonary blood flow It is suggested that syncope in Fallot s tetralogy which is always associated with gross cyanosis and virtual cessation of the pulmonary blood flow, is due either to pulmonary vasoconstriction or to overactivity of the hypertrophied infundibulum so that during systole it blocks the circulation to the lungs Such behaviour on the part of the infundibulum would be no more than an exaggeration of its function in reptiles and amphibia in which it serves as a muscular valve to protect the lungs from the full force of ventricular systole its late systolic contraction deflecting blood from the common ventricle into the systemic aorta (Keith 1924) Functional infundibular stenosis has been demonstrated by means of angiocardiography in cases of Fallot's tetralogy (Hilario Lind and Wegelius 1954) and has been observed by Brock when operating on cases with valve stenosis Pulmonary artery pressure pulses that show a late systolic trough are also highly suggestive

Physical signs

The *pulse* and *venous pressure* are usually normal but a small dominant *a* wave rising some 3 cm above *v* is seen in 20 per cent of cases giant *a* waves do not occur

The left ventricle is nearly always impalpable at the expected position of the apex beat and there is very little or no demonstrable lift over the right ventricle in 90 per cent of cases, a moderate lift occurring in the remainder A strong grade 3 right ventricular heave practically excludes Fallot s tetralogy Pulsation can never be felt in the second space over the pulmonary artery

There is always a *systolic murmur* over the outflow tract of the right ventricle maximum as a rule in the third left space but occasionally higher or lower It is loud in 85 per cent moderate in 12 per cent and soft in 3 per cent A *thrill* accompanies 85 per cent of the loud murmurs but not the others it is therefore present in nearly three quarters of all cases The murmur is caused by turbulence set up at the stricture and is not due to the shunt It is a pulmonary or infundibular ejection murmur, starting early because the pulmonary diastolic pressure is low and finishing usually just before the aortic second sound it does not spill through A_2 like the long murmur of severe pulmonary stenosis with normal aortic root

(Vogelpoel and Shrire 1955) This may be because the right ventricle empties relatively quickly, as previously described or because of total (partly functional) infundibular obstruction in late systole As might be expected the intensity and length of the murmur vary inversely with the pulmonary blood flow, and diminish greatly during spontaneous attacks of increased cyanosis with syncope the murmur usually disappears altogether (functional pulmonary atresia) Conversely after pulmonary valvotomy or infundibular resection the murmur often becomes explosive

The *second heart sound* is invariably single and usually fairly loud at the base because the root of the aorta is uncovered and it is only aortic valve closure that is heard There is no gallop no ejection click no pulmonary diastolic murmur and no mid diastolic murmur I have yet to hear a continuous murmur in Fallot's tetralogy whether due to patent ductus which must be extremely rare or to a broncho pulmonary communication Indeed such a murmur occurring in a case which has many features suggesting Fallot s tetralogy makes a diagnosis of pulmonary atresia virtually certain

Electrocardiogram

The P pulmonale is often said to be typical of Fallot s tetralogy and has been reported as occurring in 80 per cent of cases (Donzelot *et al* 1951) This statement needs tempering for it is near the margin of truth and is physiologically misleading The right ventricle is not ordinarily embarrassed in Fallot s tetralogy and needs relatively little atrial help in the 100 cases analysed here the P wave was normal in 42 per cent 2 to 2 5 mm high in the most favourable lead in 26 per cent 3 to 3 5 mm high in 25 per cent and 4 or more mm high in 7 per cent Thus in two thirds of the cases it did not exceed 2 5 mm While it is agreed therefore that a P pulmonale is common in Fallot s tetralogy its small stature and the frequency of a normal P wave are stressed for in these respects the P wave differs from its behaviour in pulmonary stenosis with reversed interatrial shunt

Right ventricular preponderance as customarily interpreted from multiple chest leads was slight in 9 per cent of cases moderate in 24 per cent considerable in 57 per cent and gross in 7 per cent the graph being normal in 3 per cent Here again the point that requires emphasis is the relatively minor change found in one third of all cases (fig 8 81) in remarkable (but expected) contrast to the findings in severe pulmonary stenosis with normal aortic root There was no convincing correlation between the grade of right ventricular preponderance and the degree of cyanosis or effort intolerance for example when right ventricular preponderance was slight or moderate one third of the cases had considerable or gross cyanosis when it was grade 3 or 4 41 per cent had considerable or gross cyanosis This is not surprising because the work of the right ventricle is the same whether cyanosis is absent or gross and whether the

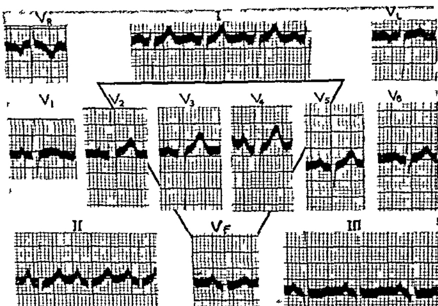


Fig 881—Electrocardiogram in a typical case of Fallot's tetralogy showing a small P pulmonale in lead 2 and only slight right ventricular preponderance

stenosis is relatively mild or extreme for it is determined by its stroke volume and the systemic peripheral vascular resistance If in fact there is some relationship between the degree of right ventricular preponderance and the size of the shunt it could only be explained by a difference in left ventricular work with a large shunt and small pulmonary blood flow the left ventricle is underfilled and therefore performs less work with little or no shunt and a relatively good pulmonary blood flow it is well filled and therefore performs more work On the whole the findings best fit the thesis (based on direct surface leads at operation) that in Fallot's tetralogy the electrocardiographic appearances at any rate in respect of QRS are due to strong clockwise rotation of the heart so that the tall R wave of lead V_1 is really left ventricular (McGregor 1950)

X ray

The skiagram is usually pathognomonic under the clinical circumstances and is characterised by conspicuously clear lung fields due to diminution of the pulmonary blood flow by a notable gap between the aortic knuckle and ventricles due to hypoplasia of the pulmonary artery and by a tip-tilted cardiac apex (fig 882) This is the cœur en sabot for it resembles the shape of a peasant's wooden shoe with turned up toe The effect is produced by considerable hypertrophy of the right ventricle with displacement of the interventricular septum to the left so that the left ventricle appears as a small cap above the right ventricular apex Occasionally the lung fields present a reticular appearance representing





(a) Anterior view (b) Second oblique position

Fig 8 82—Skiagram of a case of Fallot s tetralogy showing the cœur en sabot

development of the bronchial circulation The transverse diameter of the heart is usually normal in the anterior view In the left anterior oblique view the heart shadow may be globular owing to the increased curvature of the right atrium and ventricle If the aorta is right sided the knuckle may be seen above the right atrium (fig 8 83) and the barium filled œsophagus is deflected to the patient s left In the present series a radiological diagnosis could be made with confidence under the clinical circumstances in 70 per cent of cases pulmonary ischæmia was present in all of these a bay in the region of the pulmonary artery in 70 per cent of them (half the whole series) and a sabot shaped apex in 64 per cent of them (45 per cent of the whole series) A right sided thoracic aorta was present in 20 per cent On the other hand the appearances were strictly normal in 15 per cent (fig 8 84) and the pulmonary artery was slightly dilated in 8 5 per cent (fig 8 85) The rest were atypical



Fig 8 83—Right sided aortic arch and dorsal aorta in a case of Fallot s tetralogy

The shunt may be demonstrated by means of angiocardiography



Fig 8 84—Virtually normal sk agram in a case of acyanotic Fallot s tetralogy

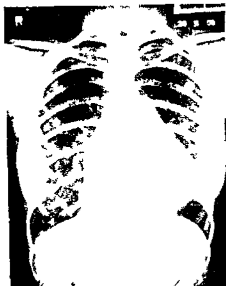


Fig 8 85—Skiagram sho ing dilatat on of the pulmonary artery a sabot shaped apex more enlargement of the right heart than usual and a very prominent inferior vena cava in a proved case of Fallot s tetralogy

I g 8 86—Angiocard ogram of a case of Fallot s tetralogy showing imultaneous opac fi cat on of th aorta and pulmonary artery The tenosis appe r to be infundibul Both pulmonary and both sub lavian art can b seen

(Grishman Steinberg and Sussman 1941) which shows immediate filling of the aorta and great vessels from the right ventricle and undersized pulmonary arteries (fig 8 86) The antero posterior view is advised in order to reveal the anatomy of both subclavian arteries—a point of interest to the surgeon using Blalock s technique

The stenosis itself is rarely seen (Lowe 1953) unless the technique is exceptionally good or selective angiocardiography is employed The medium passes through the heart quickly in Fallot s tetralogy there being no delay in the right ventricle as in pulmonary stenosis with closed ventricular septum and the pulmonary arteries themselves are always densely opacified

PHYSIOLOGICAL FINDINGS

Of 84 cases catheterised the pulmonary artery was entered in 85 per cent the aorta in 27 per cent the left atrium in 17 per cent and the left ventricle in 6 per cent When the pulmonary artery could not be reached the aorta was entered as often as not (6 out of 12 such cases) failing that it was at least possible to take immediately consecutive pressure tracings from the right ventricle and brachial or femoral artery The following observations are based on this experience

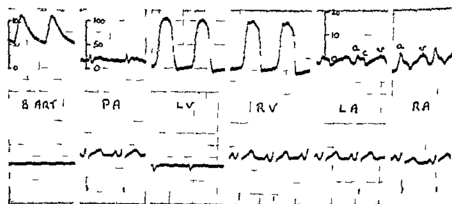


Fig 8 87—Intracardiac pressure tracing from a case of Fallot s tetralogy showing virtually identical systolic pressures in the brachial artery left ventricle and right ventricle

The characteristic findings include a low pulmonary artery pressure with a poor often deformed pressure pulse averaging 9/2 mm Hg (mean 5) above the sternal angle a right ventricular systolic pressure identical with the aortic or brachial systolic pressure under all circumstances identical or nearly identical pressures in both atria and both ventricles respectively and an *a* wave in the right atrial pressure pulse averaging only 2 to 2 5 mm Hg above *c* and never exceeding 5 mm Hg (fig 8 87) the arterial oxygen saturation ranged between 43 and 87 per cent in cyanotic cases (average 73 per cent) and between 86 and 97 per cent in acyanotic cases (average

91 4 per cent) Left atrial samples were invariably between 90 and 97 per cent saturated and averaged 93 4 per cent proving the absence of reversed interatrial shunt despite the patent foramen ovale Left ventricular sample ranged between 74 and 92 per cent saturated averaging 81 per cent in these cases the arterial oxygen saturation averaged 78 per cent proving that the shunt in Fallot s tetralogy is chiefly at ventricular level as it is in Eisenmenger s complex and not a matter of the right ventricle expelling part of its contents directly into an over riding aorta it is unlikely that any appreciable shunt takes place in diastole for if diastolic ventricular pressures favoured a right to left shunt at ventricular level they must also do so at atrial level which has already been proved untrue Bidirectional shunt was never found in cyanotic cases and only once in the acyanotic group but in three of the latter no shunt at all could be demonstrated and in one there was a unidirectional slight left to right shunt

The site of the stenosis can be recognised as high intermediate or low during cardiac catheterisation but while the last two denote infundibular stenosis it is impossible to be sure whether a high site means valve stenosis or high infundibular stenosis It is most unusual in Fallot s tetralogy to be able to reproduce the clean type of infundibular tracing obtained in the great majority of cases of infundibular stenosis with normal aortic root

In calculating the size of the shunt the pulmonary blood flow must be worked out on the assumption that pulmonary venous blood is 95 per cent saturated In the present series the systemic blood flow averaged 5 L/min and the pulmonary flow 3 L/min giving an average shunt of 2 L/min

Dye Concentration Curves

Evans blue dye reaches the ear well ahead of normal time as its rapidly built up concentration levels out or falls off it is suddenly reinforced by dye that has circulated through the lungs If the dye is injected directly into the right ventricle its immediate appearance in the ear proves that the reversed shunt is at ventricular or aorto pulmonary level not below

If an oximeter is not available saccharin or some other test substance may be injected into the right ventricle with similar qualitative results

DIFFERENTIAL DIAGNOSIS

The chief difficulty is to distinguish Fallot s tetralogy from *pulmonary stenosis with reversed interatrial shunt* In their characteristic form these two conditions are very different but when atypical may be remarkably similar (see page 417)

Pulmonary atresia is easily recognised by the absence of a pulmonary ejection murmur the almost invariable presence of a continuous murmur under one or other or both clavicles and the more conspicuous ascending aorta

Eisenmenger s complex proper with a single second heart sound and

minimal dilatation of the pulmonary artery may cause real difficulty Absence of squatting slight pulsation over the pulmonary artery, a pulmonary ejection click absence of a pulmonary systolic thrill the presence of a Roger murmur and a faint pulmonary diastolic murmur are all strongly in favour of pulmonary hypertension with reversed interventricular shunt

Acyanotic examples of Fallot s tetralogy are usually confused with *maladie de Roger* The history alone should prevent any such error for effort intolerance is at least moderate in the former and invariably absent in the latter The chief differences in the physical signs are the timing of the murmur and the character of the second heart sound the murmur is a pulmonary ejection murmur in Fallot s tetralogy a pansystolic shunt murmur in maladie de Roger the second heart sound is always single in Fallot s tetralogy split in maladie de Roger

COMPLICATIONS

Pulmonary tuberculosis complicated only 2 per cent of the cases in this series which is similar to its incidence in the general population

Cerebral abscess presumably from a small paradoxical embolism is responsible for death in about 5 per cent of all fatal cases of congenital heart disease (Robbins 1945 Gates Rogers and Edwards 1947) Fallot s tetralogy has been the primary lesion in half the reported cases The abscess which is usually solitary is not secondary to bacterial endocarditis but to some somatic infection often of a trivial nature A history of such infection however has been obtained in only a third of the cases (Sancetta and Zimmerman 1950)

Cerebral thrombosis with hemiplegia is not uncommon especially in infancy and is attributed to polycythæmia

Bacterial endocarditis is relatively uncommon probably because of the high natural mortality of most cyanotic forms of congenital heart disease in childhood and adolescence

PROGNOSIS

Uncomplicated relatively mild cases may reach middle life but the majority die young According to Campbell (1948 1950) only one patient in ten with congenital cyanotic heart disease reaches the age of 21 only one in five reaches puberty and only one in two reaches the age of 7 The most common cause of death in infancy and early childhood is undoubtedly *syncope* the mechanism of which has already been discussed *Bacterial endocarditis* and *cerebral abscess* each takes its toll of about 10 per cent and *cerebral thrombosis* may be fatal *Intercurrent infection* is probably responsible for most of the remainder not because these children are especially prone to such infections but because they tolerate them badly *Congestive heart failure* is very unusual, for as stated repeatedly the right ventricle

is not overburdened in Fallot s tetralogy According to Rich (1948) 90 per cent of fatal cases show widespread thrombotic obstruction of the small pulmonary vessels possibly due to polycythæmia Just what part this plays is open to question an increased pulmonary vascular resistance has yet to be demonstrated at catheterisation

TREATMENT

Since the operative mortality is around 30 per cent in infants under 3 years old it is wise to defer operation until the child is 5 or 6 if possible In severe cases the wait may be trying and not without its own mortality Attacks of severe dyspnœa and cyanosis with or without syncope are the chief danger For these Taussig (1948) advised placing the child in the knee chest position and if relief was not immediate giving morphine in a dose of 1 mg per kilogram of body weight which she found almost specific An oxygen tent may have to be used in the worst cases to carry the infant through a difficult period This usually increases the arterial oxygen by about 10 per cent as noted by Taussig and Blalock (1947) when oxygen was given by the anæsthetist as a preliminary to opening the thorax Operation should not be delayed after the age of 3 however if serious attacks continue

As a result of Taussig s observation that infants with Fallot s tetralogy deteriorated when the ductus arteriosus closed and that cases complicated by persistent patent ductus fared better than those without she and Blalock devised the anastomotic operation that proved so successful (Blalock and Taussig 1945 Blalock 1946 1947) One or other subclavian artery is anastomosed to the homolateral branch of the pulmonary artery Better alignment is obtained as a rule with the right subclavian but the left has a longer intrathoracic course and is therefore easier to bring down If results are poor a second anastomosis may be carried out later on the opposite side Another method of achieving the same object is to make a direct anastomosis between the aortic arch and the left pulmonary artery (Potts *et al* 1946 1948)

The physiological results of technically successful anastomosis are good cyanosis and clubbing may disappear breathlessness decreases the habit of squatting is usually given up and effort tolerance improves the arterial oxygen saturation rises to the region of 80 per cent and the blood count returns to normal (Taussig 1948) a loud machinery murmur and coarse thrill may be detected on the homolateral side immediately after the operation in nearly all cases and are permanent Blalock s total mortality rate for this operation is 17 per cent but this includes infants (mortality rate 25 per cent) cases of tricuspid atresia and other anomalies His mortality rate for selected cases of Fallot s tetralogy is not more than 10 per cent The results and mortality rate of Potts operation are much the same (Potts 1949)

Both Brock (1948) and Sellors (1948) however, proved that pulmonary stenosis was amenable to direct attack the approach being through the wall of the right ventricle Valvotomy is undertaken when the stenosis is valvular infundibular resection (Brock 1949) when the stricture is below the valve Campbell Deuchar and Brock (1954) have reported the results on the first 100 cases of Fallot s tetralogy treated by valvotomy (37 cases) infundibular resection (45 cases) or both (18 cases) at Guy s Hospital and the Brompton Hospital Two thirds of them were greatly improved one sixth were better but not in the same class and nearly one sixth died as a result of the operation the mortality from pulmonary valvotomy was stated to be 11 per cent and from infundibular resection 18 per cent Although the risk was greater with infundibular resection the results were better in those who survived Campbell and Deuchar (1953) also report the results of 200 Blalock Taussig anastomotic operations most of which were under taken for Fallot s tetralogy A comparison of the results obtained in the two types of operation by the same team is especially valuable The mortality in the anastomotic operation in Fallot s tetralogy was only 8 per cent and 75 per cent of the cases ' benefited greatly but the authors were careful to say that some incapacity usually remained and that cyanosis clubbing and polycythæmia were not as a rule abolished though much reduced The matter may be summed up by saying that the reports from Guy s indicate that the best immediate results are obtained by infundibular resection at the cost of twice the operative mortality The physiological results from pulmonary valvotomy were not quite so good but probably better than from the Blalock Taussig operation on the other and the operative mortality was a little higher

Personal experience at Brompton and elsewhere has been more or less similar but enthusiasm for the Blalock Taussig operation is difficult to maintain These patients are better than they were but none of them can be classed as excellent most of them are still somewhat cyanosed and a little clubbed and effort tolerance is still limited At the Brompton Hospital 41 direct operations have been carried out on cases of Fallot s tetralogy mostly by Sir Russell Brock There were 15 primary pulmonary valvotomies and 26 primary infundibular resections seven cases had the combined operation There were only two deaths in this series, one from valvotomy the other from infundibular resection There is no doubt at all that when the operation was technically satisfactory the results if judged by effort tolerance and disappearance of cyanosis far exceeded anything seen following Blalock s operation Excellent results of this kind were observed in at least 40 per cent more often from infundibular resection than from pulmonary valvotomy as in the Guy s group But half the excellent cases produced by infundibular resection have been trans formed into cases of ventricular septal defect with left to right shunt the pulmonary resistance remaining normal The shunt is quite considerable there is radiological pulmonary plethora and the hearts are much enlarged

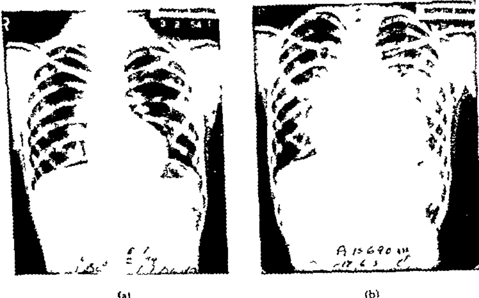


Fig 8 89—Skiagrams (a) before and (b) after infundibular resection in a case of Fallot s tetralogy showing post operative pulmonary plethora and considerable enlargement of both sides of the heart

(fig 8 88) Physiological studies in four members of this group a year or two after the operation revealed a pulmonary blood flow of 6 3 to 10 6 litres per minute (average 8 4) which was about twice the systemic flow In three of them the shunt was purely from left to right despite the over riding aorta in the fourth it may have been bidirectional for the arterial oxygen saturation was 88 per cent Right ventricular systolic pressures remained identical with those in the aorta or brachial artery the systolic pressures in the infundibular chamber and pulmonary artery were normal in two cases and raised in the other two (fig 8 89) Nothing approaching Eisenmenger s complex was ever seen The enlargement seems to be due to dilatation of both ventricles particularly the right resulting from their increased stroke volume and is greater than in simple ventricular septal defect with comparable shunt This is because the right ventricle has to pump double its normal volume at systemic pressure an uncommon physiological situation In simple ventricular septal defect with 2 1 shunt the pulmonary artery pressure is usually normal in Eisenmenger s com plex when the right ventricle is working at systemic pressure its stroke volume is usually normal

In the other half of the group with excellent results following infundibu lar resection and in all excellent results following valvotomy the physio logical situation is well nigh as perfect as it can be in the presence of a large ventricular septal defect and an over riding aorta for the two circulations appear to be delicately balanced Effort tolerance is practically

Both Brock (1948) and Sellors (1948) however, proved that pulmonary stenosis was amenable to direct attack the approach being through the wall of the right ventricle Valvotomy is undertaken when the stenosis is valvular infundibular resection (Brock 1949) when the stricture is below the valve Campbell Deuchar and Brock (1954) have reported the results on the first 100 cases of Fallot s tetralogy treated by valvotomy (37 cases) infundibular resection (45 cases) or both (18 cases) at Guy s Hospital and the Brompton Hospital Two thirds of them were greatly improved one sixth were better but not in the same class and nearly one sixth died as a result of the operation the mortality from pulmonary valvotomy was stated to be 11 per cent and from infundibular resection 18 per cent Although the risk was greater with infundibular resection the results were better in those who survived Campbell and Deuchar (1953) also report the results of 200 Blalock Taussig anastomotic operations most of which were under taken for Fallot s tetralogy A comparison of the results obtained in the *two types of operation by the same team is especially valuable* The mortality in the anastomotic operation in Fallot s tetralogy was only 8 per cent and 75 per cent of the cases 'benefited greatly but the authors were careful to say that some incapacity usually remained and that cyanosis clubbing and polycythæmia were not as a rule abolished though much reduced The matter may be summed up by saying that the reports from Guy s indicate that the best immediate results are obtained by infundibular resection at the cost of twice the operative mortality The physiological results from pulmonary valvotomy were not quite so good but probably better than from the Blalock Taussig operation on the other and the operative mortality was a little higher

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normal there is no cyanosis clubbing or polycythæmia the arterial oxygen saturation is around 90 per cent the heart is only slightly if at all larger and the pulmonary vascular shadows have improved without becoming plethoric (fig 8 90)

At operation one of the technical difficulties is to know when sufficient infundibular resection has been achieved The ideal physiological result is to restore the arterial oxygen saturation to normal without increasing the pulmonary blood flow beyond normal or at most beyond a critical safe limit (probably about 6 litres per minute at rest for a child of 10) Under the artificial conditions imposed by anæsthesia oxygen administration thoracotomy and cardiotomy much experience and fine judgment are necessary if the surgeon is to achieve this ideal he cannot rely on the

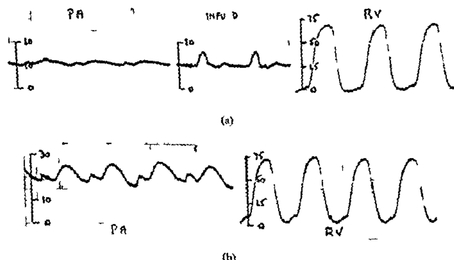


Fig 8 91—Intracardiac pressure pulse (a) before and (b) after infundibular resection in a case of Fallot s tetralogy in (b) the pressure pulse in the pulmonary artery is much better defined and at a higher level the right ventricular systolic pressure is unchanged

oximeter and can obtain no help from the right ventricular pressure which remains at systemic level under all circumstances he can however aim at producing a good pressure pulse in the pulmonary artery without an abnormal rise in pressure (fig 8 91)

There is not the same risk of over zealous surgery when undertaking pulmonary valvotomy So far there have been no examples of serious cardiac enlargement resulting from too great a shunt in this group on the contrary the difficulty has been to achieve a sufficiently good valvotomy to prevent the right to left shunt and to ensure a good pulmonary blood flow A determined attempt to split the valve efficiently however carries with it a risk of another sort that of causing serious pulmonary incompetence A pulmonary diastolic murmur has developed in one quarter of

these cases following valvotomy and in three instances the leak was by no means trivial in fact one is very serious and has led to heart failure Pulmonary incompetence is rarely important unless a left to right shunt has been created by the operation

Finally, it is hoped that all this work and controversy will prove of historical interest only for the time is already ripe for repairing the ventricular septal defect, as well as relieving the stricture under direct vision with the aid of hypothermia or some kind of artificial circulation

PULMONARY ATRESIA

Complete obliteration of the pulmonary valve and root of the main pulmonary artery accounted for 15 of the 900 cases in this series (1 7 per cent) It was always associated with a ventricular septal defect marked over riding of the aortic root and a well developed broncho pulmonary anastomosis

HÆMODYNAMICS

Life depends on the efficiency of the broncho pulmonary anastomosis rarely on the presence of a large patent ductus In those that survive infancy large bronchial arteries join one or more primary or secondary division branches of the pulmonary artery on one or both sides (Allanby *et al* 1950) Mixed venous and arterial blood from the aorta is thus carried to the lungs through the normal pulmonary arterial tree by passing only the main pulmonary trunk A less important peripheral anastomosis between the two circulations also develops The output of both ventricles is expelled entirely through the ascending aorta which is enlarged accordingly The low pulmonary vascular resistance and high feeding pressure ensures a good pulmonary blood flow if the total cross section of the communicating bronchial arteries is around 0 25 sq cm

AGE AND SEX

The average age of the patients in this small series was 11 and the range 3 to 35 years There were two males to one female

CLINICAL FEATURES

Pulmonary atresia resembles Fallot s tetralogy in many ways but it has several distinguishing features which enable it to be recognised at the bed side with ease

Cyanosis clubbing and polycythæmia are usually considerable or gross but not necessarily clinically acyanotic cases are never seen Breathlessness is considerable in two thirds and mild to moderate in one third Squatting occurred in only one quarter of the present series

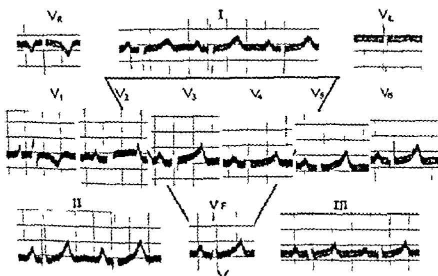


Fig 8 9 —Electrocardiogram in a case of pulmonary atresia showing relatively slight right ventricular preponderance there is a 3 mm P pulmonale in standard lead 2

One quarter also had syncopal attacks sometimes with convulsions in pulmonary atresia such attacks obviously cannot be due to transient functional occlusion of the infundibulum during systole and suggest therefore that pulmonary vasoconstriction or a fall in systemic peripheral resistance is responsible No opportunity to study an attack presented itself

The *physical signs* were like those of Fallot s tetralogy except that instead of a pulmonary ejection murmur which of course was absent there was a continuous murmur in all 15 cases It was best heard just below the clavicle and was bilateral in two thirds of the cases when it was unilateral it was as often on the right side as on the left There is good reason to believe therefore that this murmur is nearly always caused by a proximal broncho pulmonary anastomosis and not by a patent ductus

The electrocardiogram does not differ from that in Fallot s tetralogy (fig 8 9) but the skiagram usually shows a more prominent ascending aorta (fig 8 93) or knuckle Angiocardiography may reveal the broncho pulmonary anastomosis and shows no main pulmonary artery (fig 8 94)

The pulmonary blood flow may be measured very easily for it is only necessary to obtain a sample of blood from the brachial or femoral artery and to measure the oxygen consumption the mixed blood in the arterial sample is the same as that in the pulmonary arteries and pulmonary venous blood may be assumed to be 95 per cent saturated In the few that have been measured the pulmonary blood flow has ranged between 2 and 4 litres per minute

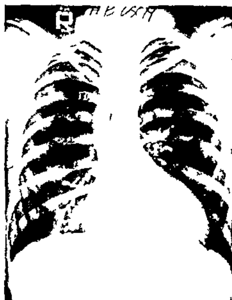


Fig 8 93—Skiagram from a case of pulmonary atresia showing a prominent ascending aorta conspicuous pulmonary bay and pulmonary ischæmia Angiocardiography proved that the aortic arch and dorsal aorta were left sided



Fig 8 94—Angiocardiogram from a case of pulmonary atresia showing dense opacification of the right ventricle and aorta and a large broncho pulmonary anastomotic vessel on the left side

The *prognosis* in those who survive infancy seems much the same as in Fallot s tetralogy

Surgical treatment is not nearly so satisfactory as in Fallot s tetralogy, and the mortality is higher Blalock s operation is usually advised if the pulmonary blood flow is below 4 litres per minute Considerable care must be taken not to interfere with the broncho pulmonary shunt particularly if unilateral while constructing the artificial anastomosis

ABSENT LEFT OR RIGHT BRANCH OF THE PULMONARY ARTERY

From time to time cases are seen in which the pulmonary vascular markings are very light on one side and unduly heavy on the other When there is no kyphoscoliosis and no evidence of unilateral emphysema this usually means congenital absence of the left or right pulmonary artery The whole of the right ventricular output passes down the normal branch as it does following pneumonectomy There is no rise in resting pulmonary artery pressure because the flow is only twice normal but there is less reserve and the pressure may well rise on exercise The ischæmic lung handles about one third of the inspired air but takes up only 6 per cent of the total oxygen uptake (McKim and Wiglesworth 1954)

As a rule the aortic arch is on the side opposite that of the absent pulmonary artery The deficiency may be associated with other congenital anomalies such as Fallot s tetralogy (Nadas *et al* 1953) when it may have an important bearing on the surgical treatment

TRICUSPID ATRESIA

Tricuspid atresia accounted for 1 5 per cent of the 900 cases analysed here Uncomplicated cases (type I of Edwards and Burchell 1949) have an atrial septal defect or patent foramen ovale through which blood escapes from the otherwise closed right atrium into the left atrium blood reaches the lungs from the left side of the heart through a ventricular septal defect patent ductus or broncho pulmonary anastomosis In addition there may be pulmonary atresia or stenosis valvular or infundibular Complicated cases (type II of Edwards and Burchell 1949) have transposition of the great vessels with or without pulmonary stenosis venous blood entering the left atrium via the foramen ovale mixes with blood from the lungs and passes directly into the pulmonary artery and indirectly into the aorta via a ventricular septal defect *In either case the left ventricle does all or most* of the work but the lungs are ischæmic in type I plethoric in type II

AGE AND SEX

Of 37 cases mostly collected from the literature 28 died within the first year three within the second year and six between the ages of 2 and 5 (Sommers and Johnston 1951) The average age of the 13 cases described here however was 9 4 years and the range 3 to 17

The sexes are fairly equally represented perhaps with a slight bias in favour of females (M/F=4/5)

CLINICAL FEATURES

Effort intolerance cyanosis clubbing and polycythæmia are invariably considerable or gross squatting is the rule angina occasional and syncope rare

The physical signs include a giant a wave when there is a foramen ovale rather than an atrial septal defect a forceful left ventricular cardiac impulse a systolic murmur usually accompanied by a thrill at the base due to ventricular septal defect in over half the cases and a single second heart sound owing to absence of the pulmonary element in the majority Sometimes there is only a trivial aortic flow murmur at the base and a continuous murmur under the left clavicle which in tricuspid atresia is more likely to be caused by a patent ductus than by a broncho pulmonary anastomosis Occasionally the second heart sound is split especially when there is a good sized ventricular septal defect the pulmonary element can be very late when there is associated pulmonary stenosis

Fig 8 95—Electrocardiogram in a case of tricuspid atresia showing considerable left ventricular preponderance

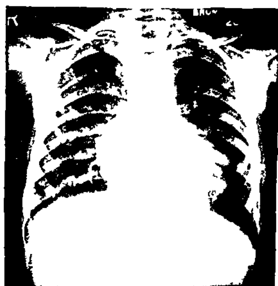


Fig 8 96—Tricuspid atresia showing pulmonary ischæmia with enlargement of the right atrium and left ventricle

The *electrocardiogram* is characterised by a conspicuous P pulmonale averaging 3.5 to 4 mm in amplitude and grade 2 to 3 left ventricular preponderance (fig 8 95)

X rays show a combination of pulmonary ischæmia hypoplastic pulmonary artery left ventricular enlargement and dilatation of the right atrium (fig 8 96)

Angiocardiography shows diagnol filling the two atria in high concentration almost simultaneously followed by opacification of the left ventricle and aorta the pulmonary artery remaining invisible or but faintly delineated (fig 8 97)

Cardiac catheterisation is not advised because it can only reveal a giant *a* wave in the right atrium and reversed interatrial shunt findings which do not exclude pulmonary hypertension or stenosis with reversed inter atrial shunt Failure to pass the catheter through the tricuspid orifice is no evidence of atresia

The *prognosis* is poor most patients dying in infancy Blalock s or Pott s operation may greatly improve the pulmonary blood flow and so relieve cyanosis and dyspnœa but the shunt adds to the burden of the left ventricle and may lead to heart failure Nevertheless surgical treatment is well worth while despite a fairly high mortality

TRANSPOSITION OF THE GREAT VESSELS

Transposition the aorta rising anteriorly from the right ventricle and the pulmonary artery posteriorly from the left ventricle occurred in 1 per cent of these 900 congenital cases and in 6 9 per cent of Abbott s series It is a relatively common form of cyanotic congenital heart disease in infancy (Astley and Parsons 1952) but few patients survive Obviously if the two circuits are closed and independent life cannot be sustained Clinical cases therefore must have some means whereby blood is transferred from the systemic to the pulmonary circuit and vice versa ventricular and atrial septal defects usually provide these means blood entering the pulmonary circulation through a ventricular septal defect and leaving it via an atrial septal defect Cases may be further complicated by a high pulmonary vascular resistance pulmonary stenosis tricuspid atresia or other anomalies

HÆMODYNAMICS

If the pulmonary vascular resistance is more or less normal a ventricular septal defect allows venous blood from the right ventricle to enter the left ventricle and pulmonary artery where it mixes with oxygenated blood from the left atrium If these is no atrial septal defect the pulmonary circulation is flooded the only escape being through bronchial anastomotic veins With an atrial septal defect the pulmonary circulation is still plethoric but less so oxygenated blood escaping into the right atrium an



(a)



(b)



( )



(d)

Fig 8 97—Angiocardiogram in a case of tricuspid atresia showing (a) diodone passing directly into th left atrium (1 second) (b) early filling of the left ventricle and aorta (2 seconds) (c) in the second oblique position the left side of the heart and aorta are filled in 2 second (d) at 3 seconds a small left pulmonary artery is becoming visible Note bronchial collaterals in right upper zone in (b)

so to the right ventricle and aorta In otherwise uncomplicated cases there may be hyperkinetic pulmonary hypertension and samples from the pulmonary artery are always more saturated with oxygen than samples from the aorta

If the pulmonary vascular resistance is raised or if there is associated pulmonary stenosis the right to left interventricular shunt is limited or reversed according to the degree of obstruction to pulmonary flow the interatrial shunt is adjusted accordingly being proportionately limited or reversed respectively When the shunts are reversed venous blood from the right atrium enters the left atrium through the atrial septal defect and after mixing with oxygenated blood from the lungs passes on to the left ventricle part of this mixed blood then enters the pulmonary artery and part is shunted into the right ventricle and aorta through the V S D Under these circumstances the pulmonary blood flow is diminished although samples from the pulmonary artery are still more oxygenated than samples from the aorta Tricuspid atresia complicating transposition causes similar reversed shunting through both septal defects

Finally when the defects are large bidirectional shunts may occur at atrial or ventricular level

AGE AND SEX

The average age of the eight patients in this small series was 13 years and the range 3 to 33 years The sexes were equally represented

CLINICAL FEATURES

Effort intolerance, cyanosis, clubbing and polycythæmia were moderate to gross squatting was noticed in only one instance and in only four of 25 cases reported by Campbell and Suzman (1951) Neither angina pectoris nor syncope occurred

The *physical signs* vary according to the chief complication The pulse and venous pressure are usually normal but the jugular pulse may show a small dominant *a* wave The cardiac impulse is usually right ventricular in type a moderate systolic thrust extending from the left sternal edge towards the mid clavicular line In about a quarter of the cases there is no murmur at all in some there is a Roger murmur and thrill and in others a pulmonary ejection murmur and thrill particularly in those with pulmonary stenosis Continuous murmurs are very rare if they occur at all even in those with patent ductus A pulmonary diastolic murmur may be heard when the pulmonary vascular resistance is high and a functional mitral diastolic murmur when there is marked pulmonary plethora The second heart sound also varies according to the nature of the chief complication As a rule it is loud because the root of the aorta is anterior and uncovered by the pulmonary artery In about a third of the cases it r cognisably split and when the pulmo [illegible] lar resistance is ra



(a)



(b)



(c)



(d)

Fig 8 97— Angiocardiogram in a case of tricuspid atresia showing (a) diodone passing directly into the left atrium (1 second) (b) early filling of the left ventricle and aorta (2 seconds) (c) in the second oblique position the left side of the heart and aorta are filled in 2 seconds (d) at 3 seconds a small left pulmonary artery is becoming visible Note bronchial collaterals in right upper zone in (b)

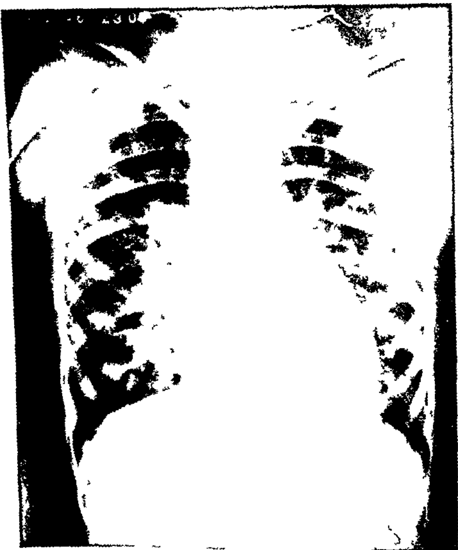


Fig. 8.20 — Skiagram of a case of transposition of the great vessels associated with atrial and ventricular septal defects



Fig 8 100—Angiocardiogram in a case of transposition showing a convex arc high up on the left border of the heart this is the ascending aorta and not the pulmonary artery

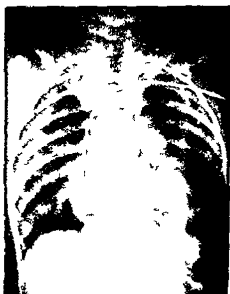


Fig 8 101—Case of transposition of the great vessels showing the typical position of a catheter which has been passed up the ascending aorta and round the aortic arch

to the nature of the associated anomalies As a rule there is a left to right shunt at atrial level if there is an atrial septal defect and a right to left shunt at ventricular level with ventricular septal defect but either shunt may be bidirectional or reversed particularly if there is a raised pulmonary vascular resistance or pulmonary stenosis with tricuspid atresia both shunts are entirely reversed Pressures in the right ventricle and pulmonary artery depend on the pulmonary blood flow the pulmonary vascular resistance and the degree of pulmonary stenosis if present The pulmonary blood flow is high in relatively uncomplicated cases, even when the shunts are small for there is a large volume of oxygenated blood permanently trapped in the pulmonary circulation it may be only slightly in excess of normal however when the pulmonary vascular resistance is high or when there is severe pulmonary stenosis

DIFFERENTIAL DIAGNOSIS

The triad comprising central cyanosis unquestionable pulmonary plethora and right ventricular dominance usually means transposition of the great vessels or *total anomalous pulmonary venous drainage* into the right side of the heart and these two can usually be distinguished radiologically *Persistent truncus* with cyanosis and pulmonary plethora is at once recognised by the large left ventricle

When pulmonary plethora is unconvincing because of associated pul

monary stenosis there may be great clinical difficulty in distinguishing transposition from *Fallot's tetralogy* with a relatively good pulmonary blood flow in fact the only real differences between them are the degree of cyanosis which in transposition is considerable and in Fallot's tetralogy of this kind slight and the size of the heart which is usually larger in transposition If angiocardiography shows no filling of the pulmonary artery *pulmonary atresia* may be diagnosed in error but this mistake should not be made at the bedside

When pulmonary plethora is doubtful because the pulmonary vascular resistance is raised transposition is commonly confused with *Eisenmenger's complex* Genuine dilatation of the pulmonary artery favours Eisenmenger's complex but angiocardiography or cardiac catheterisation may be necessary to establish the diagnosis with certainty

PROGNOSIS

The average duration of life in 123 cases with associated anomalies of the kind described above was 19 months (Hanlon and Blalock 1948) without such associated anomalies life is impossible The patients in the present series however had already survived infancy and their ages show that with good communications between the two circulations the immediate outlook is far from hopeless 9 out of 25 cases of probable transposition reported by Campbell and Suzman (1951) were between 6 and 18 years of age the rest being under 5

TREATMENT

So far attempts to improve the efficiency of communications between the two circulations such as the creation of an artificial atrial septal defect (Blalock and Hanlon 1950) have proved disappointing Surgical correction of the transposition itself with the aid of some form of artificial circulation to the brain is still in the experimental stage

PERSISTENT TRUNCUS ARTERIOSUS

Persistent truncus results from failure of development of the aorto pulmonary septum so that a single large vessel arises from both ventricles The solitary valve usually has four cusps and a ventricular septal defect is inevitable The pulmonary arteries should arise from the common trunk and if they fail to do so the probable diagnosis is pulmonary atresia

Persistent truncus is a very rare anomaly and there was but one proved example amongst the 900 congenital cases reported here

HÆMODYNAMICS

If the pulmonary vascular resistance is normal the pulmonary circulation is flooded to its maximum capacity because the pulmonary arteries are filled at systemic pressure The left ventricle enlarges greatly to

the torrential flow that is received from the lungs and the right ventricle hypertrophies to adapt itself to systemic conditions The truncus itself may be very large not simply because it represents two great vessels but because it may have to carry an enormous flow Cyanosis may be minimal because *mixed venous blood from the systemic and pulmonary circulations* is about five sixths pulmonary and therefore likely to be well over 80 per cent saturated

A normal pulmonary vascular resistance however may be unusual in cases that survive infancy and physiological studies may well reveal a resistance in the Eisenmenger range (around 17 units) in the majority Pulmonary and systemic blood flows would then be balanced and the two ventricles would perform identical work Cyanosis should be considerable in this group

If the pulmonary resistance rose much above systemic level the pulmonary blood flow would be diminished and the left ventricle would perform less work than the right Such cases would be intensely cyanosed and similar physiologically to pulmonary atresia

CLINICAL FEATURES



Fig 8 102—Case of persistent truncus arteriosus showing marked pulmonary plethora a conspicuous bay in the region of the pulmonary artery and considerable enlargement of the heart shado due chiefly to dilatation of the left ventricle

Persistent truncus with a relatively normal pulmonary vascular resistance is characterised by slight central cyanosis clubbing and polycythæmia and relatively slight effort intolerance until there is left ventricular failure the pulse may be water hammer in quality and there may be a small dominant *a* wave in the jugular venous pulse but the venous pressure is usually normal until heart failure develops the left ventricle is thoroughly enlarged and hyperdynamic the right less so *there is usually a systolic ejection* murmur with or without thrill at *the base* a loud single second sound and sometimes a basal diastolic murmur due to a leaking quadricuspid valve the incompetence affecting both ventricles A functional mitral diastolic murmur would be expected A continuous broncho-pulmonary anastomotic murmur means pulmonary atresia, not persistent truncus

The electrocardiogram shows conspicuous Q waves and tall R waves in leads V_5 and V_6 and perhaps a secondary R wave in leads V_1 and V from right ventricular hypertrophy as well The P wave may be normal bifid and widened from left atrial enlargement or a little tall and sharp from right atrial hypertrophy

The skiagram shows gross pulmonary plethora absence of the pulmonary arc a conspicuous ascending aorta and considerable enlargement of the heart shadow particularly the left ventricle (fig 8 102)

When the pulmonary vascular resistance is high the clinical features are more like Eisenmenger s complex Cyanosis and clubbing are much more conspicuous and dyspnœa more severe The pulse loses its water hammer quality The ventricles are about equal in size and clinically the right may be dominant Auscultatory signs are unchanged except that a mitral diastolic murmur would not be expected The electrocardiogram shows a P pulmonale and considerable right ventricular preponderance Radiologically there is less pulmonary plethora (if any) and less cardiac enlargement whilst the left ventricle is no longer hyperdynamic

DIFFERENTIAL DIAGNOSIS

Many cases of persistent truncus present clinical electrocardiographic and radiological features that lie somewhere between the two prototypes described above Essentially the pattern is one of central cyanosis enlargement of both ventricles particularly the left a single second heart sound absence of the pulmonary arc and pulmonary plethora This combination admits of no other diagnosis

Pulmonary atresia with its continuous broncho pulmonary anastomotic murmur small quiet left ventricle and obvious pulmonary ischæmia presents an entirely different picture and should not enter into the differential diagnosis at all

Eisenmenger s complex can nearly always be distinguished by the dilated pulmonary artery *Transposition* alone presents any real difficulty Both it and persistent truncus have central cyanosis pulmonary plethora and a hyperdynamic left heart but in transposition the second heart sound may be split the ascending aorta is inconspicuous or in its wrong position and the right ventricle is nearly always dominant

Angiocardiography should reveal the essential anatomical arrangement in persistent truncus On *cardiac catheterisation* the pathognomic finding is to enter either pulmonary artery from the ascending aorta In the case studied in this series there was no difficulty in accomplishing this pulmonary artery aortic and right ventricular systolic pressures were identical the oxygen saturation of samples was 48 per cent in the right atrium 58 per cent in the right ventricle and 72 per cent in the truncus proving the presence of a left to right shunt at ventriculo aortic level

PROGNOSIS AND TREATMENT

Cases with a low pulmonary vascular resistance probably die from cardiac failure in infancy When the pulmonary resistance is raised sufficiently to protect the lungs from over flooding and the left ventricle from overwork but not so much as to diminish the pulmonary blood flow the outlook is not so bad and may be more like that in Eisenmenger s complex As a general rule however patients who survive infancy die from congestive heart failure in childhood or adolescence No surgical treatment is possible

TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE

Embryologically a single pulmonary vein originally joins the sinus venosus The superior horns of the sinus ducts of Cuvier and lower part of the anterior cardinal veins become the superior vena cava on the right side and the oblique vein of the left atrium (vein of Marshall) and coronary sinus on the left A persistent left superior vena cava therefore joins the oblique vein of the left atrium and enters the right atrium via the coronary sinus

The formation of the interatrial septum separates that part of the sinus venosus that the pulmonary vein joins from the rest of the right atrium Since there are normally four pulmonary veins joining the left atrium it is clear that the original single pulmonary venous trunk becomes absorbed into the sinus venosus It is not at all difficult for one or other of the right pulmonary veins to find itself entering the primitive atria on the wrong side of the growing septum *Partial anomalous pulmonary venous drainage* arising in this way has already been described and is not infrequently associated with atrial septal defect

In total anomalous pulmonary venous drainage the original single pulmonary vein may join up with almost any other part of the sinus venosus system thus it is found entering the coronary sinus in 19 per cent left superior vena cava in 43 per cent, right superior vena cava in 12 per cent right atrium in 14 per cent and even the inferior vena cava sometimes (Keith *et al* 1954) When it enters the coronary sinus there is usually a left superior vena cava as well and this invariably communicates with the left innominate vein and so with the right superior vena cava through which the pulmonary venous blood eventually drains into the right atrium

HÆMODYNAMICS

All the blood from the lungs enters the right atrium by one route or another, and after mixing with blood from the systemic veins passes to the left ventricle via an atrial septal defect or foramen ovale, and to the right ventricle through the tricuspid valve Samples from all cardiac chambers are therefore identical

Since the right ventricle offers less resistance to filling than the left and since the tricuspid valve opening is usually wider than that in the atrial septum more blood enters the right ventricle than the left The pulmonary blood flow is therefore increased, and the systemic output tends to be low This also means that the majority of blood entering the right atrium is already 95 per cent saturated so that the mixed venous sample arriving in the left ventricle is likely to be around 85 per cent saturated Central cyanosis is therefore slight or even absent at rest If the pulmonary vascular resistance is raised the right ventricular diastolic pressure tends to rise the right to left interatrial shunt increases the pulmonary blood flow is reduced and cyanosis may then be intense but this is unusual

There were only two proved examples of this rare anomaly in the present series But five typical cases were described by Snellen and Albers (1952) four by Gardner and Oram (1953) six by Whitaker (1954) and fourteen by Keith *et al* (1954) who also reviewed 45 other cases culled from the literature A good earlier review is that by Brody (1942)

The majority of cases in the literature occurred in infancy 80 per cent proving fatal within the first year of life

The sex ratio is three males to two females

CLINICAL FEATURES

There is a very great discrepancy between the high infant mortality in this condition and the relatively good health of many classical cases described in adolescents and young adults The explanation of course lies with the behaviour of the foramen ovale or with the size of the inter atrial communication Many infants die because the foramen ovale becomes sealed off despite the higher pressure on the right side of the atrial septum (Taussig 1947) Others in whom the foramen ovale remains patent have to depend on this small opening for the whole of their systemic blood flow On the other hand patients with a good sized atrial septal defect are likely to have an adequate right to left interatrial shunt and fare relatively well (Snellen and Albers 1952) The syndrome to be described is that seen in children and young adults with good interatrial shunts

Effort intolerance is not severe and cyanosis is minimal unless the pulmonary vascular resistance is high. Recurrent bronchitis may occur as in other cases with plethoric lungs Physical development is poor

The peripheral pulse is small and the jugular venous pressure and pulse normal unless the pulmonary vascular resistance is raised (Eisenmenger reaction) or the right heart fails

The central cardiac signs are very similar to those of atrial septal defect the left ventricle is impalpable, the right thrusting and hyperdynamic and an impulse may be felt over the pulmonary artery there is nearly always a pulmonary ejection murmur in the third left space often accompanied by a faint or moderate thrill and the second heart sound is widely split and presumably unaltered by respiration the intensity of P_2 no doubt

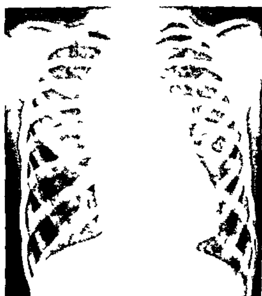


Fig 8 103—Typical figure of eight appearance in a case of total anomalous pulmonary venous drainage into the left superior vena cava

varies with the pulmonary artery pressure pulmonary incompetence occurs in a minority A superior vena caval hum uninfluenced by posture or compressing the root of either jugular vein may be heard in the aortic area in about a quarter of the cases (Snellen and Albers 1952) A functional mid diastolic murmur caused by interatrial or tricuspid turbulence was heard in three out of four cases reported by Gardner and Oram (1953) and in two out of six cases described by Whitaker (1954)

The *electrocardiogram* shows a partial right bundle branch block pattern as in atrial septal defect

The *skiagram* reveals a figure of eight appearance (fig 8 103) the upper half of which represents the dilated left superior vena cava left innominate vein and right superior vena cava as first clearly illustrated by Taussig (1947) and emphasised by Snellen and Albers (1952) Other features include a small aorta, pulmonary plethora and dilatation of the pulmonary artery right ventricle and right atrium as in atrial septal defect

Routine *angiocardiography* shows more or less simultaneous filling of both sides of the heart the reversed shunt being at atrial level after passing through the lungs contrast medium enters the left superior vena cava A clearer picture of the anomalous pulmonary venous drainage is obtained if diaginol is injected directly into the pulmonary artery

The *physiological findings* are also pathognomonic for samples from all intracardiac chambers and from both the aorta and pulmonary artery are identical or if the interatrial communication cannot be penetrated then at

least the arterial sample is the same as those from the right side of the heart S V C samples are more saturated than those from the right atrium and much more so than those from the I V C If the catheter is passed up the left subclavian vein it may enter the left superior vena cava and then fully saturated pulmonary venous blood may be obtained The pulmonary blood flow is usually over 15 litres per minute unless the pulmonary vascular resistance is raised the systemic flow averaging around 4 litres per minute The pulmonary artery pressure is usually raised moderately owing to the very great flow

DIFFERENTIAL DIAGNOSIS

The combination of slight central cyanosis otherwise typical clinical features of a large atrial septal defect with direct shunt the addition sometimes of a basal venous hum and the pathognomonic figure of eight skiagram, can hardly be mistaken for any other condition At the bedside however, atrial septal defect with bidirectional shunt despite the absence of a high pulmonary vascular resistance and cases of single atrium present very similar features Selective angiocardiography and cardiac catheterisation should establish the diagnosis with certainty

PROGNOSIS AND TREATMENT

As already stated if the foramen ovale closes or tends to close infants necessarily die but if there is a good sized atrial septal defect the outlook is fair most such cases reaching adult life although very few have been reported over 30 years old

Surgical transplantation of the misplaced pulmonary vein has yet to be accomplished

ANOMALOUS DRAINAGE OF THE S V C OR I V C INTO THE LEFT ATRIUM

A rare but interesting anomaly seen only once in this series is anomalous drainage of the superior vena cava into the left atrium The patient was a girl aged 10 with life long slight central cyanosis and grade I effort intolerance There were no obviously abnormal physical signs but the left ventricle was a little thrusting for it was working harder than the right and the second heart sound was single A being slightly later and P earlier than normal The electrocardiogram showed an S wave in lead V measuring 28 mm but was otherwise normal The skiagram looked normal Angiocardiography however revealed anomalous superior vena cava drainage into the left atrium diaginol passing directly into the left side of the heart without entering the right atrium at all (fig 8 104a) When diaginol was injected into the saphenous vein the inferior vena cava was seen to join the right atrium normally (fig 8 104b) On cardiac




(a) (b)

Fig 8 104—Angiocardiogram from a case of anomalous drainage of the superior vena cava into the left atrium (a) showing diaginol in the superior vena cava left atrium left atrial appendage left ventricle and aorta (b) showing diaginol in the right atrium right ventricle and pulmonary arteries after being injected into the saphenous vein the top of the right atrium ends blindly

catheterisation it was not at first realised that the catheter had entered the left atrium directly its immediate passage into a pulmonary vein being attributed to the presence of an atrial septal defect when a ventricle was entered the bluish sample obtained (70 per cent saturated) suggested that it was the right ventricle although its systolic pressure was at systemic level and it was of course the left

Surgical correction should be possible but the disability was too slight in this case to warrant interference

A good example of a case in which the *inferior vena cava drained directly into the left atrium* was reported by Gardner and Cole (1955) This patient died suddenly at the age of 32 and necropsy showed an old posterior cardiac infarct in addition to the anomaly under consideration The clinical features of the congenital anomaly were essentially the same as in the case of anomalous superior vena cava drainage described above there being central cyanosis without other abnormal physical signs and the skiagram also looked normal The electrocardiogram was influenced by the old infarct

COR TRILOCULARE BIATRIATUM

Hearts with two normal atria and a single ventricle are rare (1 3 per cent of Abbott s 1,000 cases) but not so rare as two chambered hearts Trans

position of the great vessels the aorta lying anteriorly and a little to the right the pulmonary artery posteriorly and a little to the left without any spiral arrangement is usually associated A rudimentary outflow chamber from which either the aorta or pulmonary artery (or both) may arise is sometimes found (Taussig 1947) and pulmonary valve stenosis is not uncommon The famous Holmes heart was from a moderately cyanosed man of 23 who died after a bout of dissipation for which he had a turn The pulmonary artery arose anteriorly from a small rudimentary outflow chamber protected proximally by an infundibular stenosis which clearly limited the blood flow to the lungs the aorta arose posteriorly from the body of the common ventricle there being no transposition in this case (Abbott 1901)

Complete mixing of systemic and pulmonary venous blood takes place in the common ventricle from which it is ejected at systemic pressure If the pulmonary vascular resistance were normal the lungs would be flooded and survival unlikely as in persistent truncus arteriosus therefore fœtal pulmonary vasoconstriction is usually maintained and this regulates the amount of blood sent to the lungs (Rogers and Edwards 1951) Pulmonary stenosis usually valvular occurs in about a quarter of all cases (Campbell Reynolds and Trounce 1953) and performs a similar service When the lungs are flooded cyanosis is minimal or absent but the single ventricle which has to perform double work under the best conditions becomes grossly overloaded When the aorta arises from a rudimentary outflow chamber with proximal stenosis extreme pulmonary vasoconstriction would be necessary to provide an adequate systemic blood flow and prevent gross flooding of the lungs

AGE AND SEX

Although the majority die in infancy probably as a result of other anomalies or because the pulmonary arterioles fail to regulate the pulmonary flow satisfactorily about 20 per cent reach adult age the oldest recorded being 56 (Mehta and Hewlett, 1945)

The sex ratio is 3 2 in favour of males (Campbell Reynolds and Trounce 1953)

CLINICAL FEATURES

The degree of dyspnœa and cyanosis is probably proportional to the pulmonary vascular resistance or to the degree of pulmonary stenosis when that is present Nevertheless slight to moderate cyanosis is physiologically desirable for acyanotic cases are far more likely to die in infancy from heart failure due to overloading of the single ventricle secondary to a flooded pulmonary circulation

No good descriptions of the physical signs of patients with single ventricle are available in the medical literature but most have a basal

systolic murmur with or without thrill and this is probably a pulmonary ejection murmur as in Eisenmenger's complex which these cases imitate closely When there is associated pulmonary stenosis the physical signs are presumably more like those of Fallot's tetralogy

The electrocardiogram is variable normal Q waves are usually seen in antero lateral chest leads or in one of the left sided unipolar limb leads despite the absence of the interventricular septum as in the univentricular heart of fishes and frogs (Kisch 1949) otherwise the graph is apt to show changes which might ordinarily be more easily attributed to clockwise or anticlockwise rotation In cases with pulmonary stenosis Campbell Reynolds and Trounce (1953) could not distinguish the graph from that seen in Fallot's tetralogy

The skiagram resembles that in Eisenmenger's complex when there is pulmonary hypertension and Fallot's tetralogy when there is pulmonary stenosis but in both types the heart is apt to be larger

Few physiological studies have yet been reported In uncomplicated cases the findings are similar to those of Eisenmenger's complex with bidirectional shunt but there is no difference between samples from the aorta and from the pulmonary artery When there is pulmonary stenosis the findings are like those in Fallot's tetralogy in respect of the pressures recorded and like uncomplicated single ventricle in respect of the samples

Angiocardiography shows simultaneous filling of the aorta and pulmonary artery as in Eisenmenger's complex and Fallot's tetralogy but with good technique it should be possible to demonstrate complete opacification of the whole ventricular shadow from the right atrium the left atrium remaining translucent

PROGNOSIS AND TREATMENT

The outlook is fair in those who survive infancy and depends on how satisfactorily the pulmonary circulation can be regulated by the pulmonary vascular resistance or the pulmonary stenosis

Surgical treatment is impossible in those with pulmonary hypertension and usually inadvisable in those with pulmonary stenosis unless the pulmonary blood flow is obviously inadequate

COR BIVENTRICULARE TRILOCULARE

Hearts with a single atrium and two ventricles are exceptionally rare They cannot be distinguished clinically from those rare cases of atrial septal defect with bidirectional but predominantly left to right interatrial shunt and a normal pulmonary vascular resistance Cardiac catheterisation however, should show identical samples from all cardiac chambers beyond the superior vena cava and inferior vena cava as if all the pulmonary veins drained directly into the right atrium The pulmonary blood flow is greatly increased because the right ventricle offers less resistance to filling than the left

The prognosis is similar to that in cases of gross atrial septal defect the few examples reported usually dying from heart failure in childhood or adolescence (Brown 1950)

No surgical treatment is possible unless an artificial septum could be created

COR BILOCULARE

A two chambered heart is probably the rarest of all congenital cardiopathies and practically never occurs without other anomalies (Brown 1950) Physiologically the situation should be precisely the same as that in a heart with two atria and a single ventricle except that mixing of pulmonary and systemic venous blood takes place in the atrium instead of the ventricle

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CHAPTER IX

RHEUMATIC FEVER AND ACTIVE RHEUMATIC CARDITIS

RHEUMATIC fever is a particular form of polyarthritis following streptococcal infection its hall marks are pancarditis chorea, sub cutaneous nodules and erythema marginatum. It may be acute sub acute or chronic

INCIDENCE

According to the 1927 report of the Child Life Committee of the Medical Research Council Social Conditions and Acute Rheumatism 10 to 15 per cent of all children at 12 years of age in England are affected by rheumatism Of 22 800 children under 15 years of age card indexed by the London County Council 2 6 per cent had had rheumatic fever (Bach *et al* 1939) The crude annual death rate from rheumatic fever declined from 67 per million persons in 1901 to 22 per million in 1937 (Glover 1939) During 1937 according to Glover rheumatic fever accounted for 2 3 per cent of all deaths in children between the ages of 5 and 9 years

The disease is rare in infancy and in old age and is most common in childhood and adolescence attacking the poor rather than the rich and having an incidence climatically and geographically parallel to streptococcal tonsillitis (Coburn 1931) The peak incidence is in children between the ages of 6 and 12 particularly during the months of October November and of January February Apart from arachnodactyly there is no evidence that a particular physical type is predisposed to rheumatic fever (Hill and Allan 1929) but hereditary predisposition is now accepted (Wilson 1940 Wilson and Schweitzer 1954)

THE NATURE OF THE RHEUMATIC STATE

There is no evidence as yet that rheumatic fever is caused directly by any infective agent Cultures from blood joint fluid pericardial or pleural effusions and from affected tissues are bacteriologically sterile and filtrates from similar samples are incapable of transmitting the disease when inoculated into animal or man There is still perhaps a remote possibility that a virus is responsible but the known facts are against it

On the other hand the evidence that rheumatic fever is intimately related to streptococcal infection is beyond dispute The relationship was first propounded by Poynton and Payne in 1900 They isolated a diplococcus from blood and other cultures and produced polyarthritis and carditis injecting it into animals but the lesions were shown later to be infe

not rheumatic However they confirmed the observation of Haig Brown (1886) that rheumatic fever was nearly always preceded by streptococcal sore throat the latent interval being 10 to 20 days (Poynton and Payne 1913) The most convincing proof of this was later given by Schlesinger (1930) The responsible organism is always a hæmolytic streptococcus (Collis 1931) As previously stated the incidence of rheumatic fever follows closely the geographic social and seasonal incidence of streptococcal tonsillitis (Coburn 1931) and small epidemics of rheumatic fever in closed communities always follow epidemics of streptococcal sore throat (Glover 1930) Culpable streptococci belong serologically to group A, and may liberate powerful erythrogenic toxins and hæmolysins—in fact they are often scarlatinal strains (Coburn and Pauli 1935) Serum from the subjects of rheumatic fever agglutinate these strains in high titre and anti streptococcal hæmolysins (antibodies excited by the antigenic properties of streptococcal hæmolysins) have been found in high titre in the early stages of practically all cases of active rheumatic fever, whether or not a history of streptococcal infection is obtained (Todd 1932) Most of these observations have been confirmed independently by other workers notably Griffith (1935) Sheldon (1931) and Bradley (1932)

It is now generally believed that rheumatic fever is an abnormal tissue reaction to the products of hæmolytic streptococcal infection in a sensitised individual A number of other observations supports this hypothesis Thus allergic polyarthritis with a latent interval of 8 to 9 days, may follow the injection of foreign serum polyarthritis may similarly follow gonococcal dysenteric and other bacterial infections in individuals sensitised by previous attacks associated skin lesions in rheumatic fever, such as erythema multiforme strongly suggest allergy The experimental work of Rich and Gregory (1943 1944) who succeeded in producing carditis of the rheumatic type in rabbits by injecting horse serum and of Cavelti (1947) who was equally successful in rats which were injected with an antigen consisting of killed streptococci and heart or connective tissue emulsion provides convincing evidence of the existence of an allergic form of carditis which may be related to the streptococcus and which at least resembles that seen in rheumatic fever Finally, Murphy and Swift (1949) produced microscopic lesions in the hearts of rabbits closely resembling those seen in rheumatic carditis, by repeated intradermal injections of group A beta hæmolytic streptococci

The relationship between rheumatic fever and rheumatoid arthritis is still uncertain Serum from patients with rheumatoid arthritis commonly agglutinates all strains of hæmolytic streptococci in high dilution (Dawson *et al* 1932) but does not, as a rule, contain the high titre anti hæmolysins characteristic of rheumatic fever (Stuart Harris 1935) nevertheless the anti streptolysin titre is much higher than in normal controls (Goldie and Griffiths 1936) Whether there is any essential difference between the pathology of the affected joints and in the structure of subcutaneous nodules

in the two conditions other than those which might be due to the age of the patient or to the chronicity of the lesion, is still a matter of controversy (Goldie 1936) The incidence of a rheumatic type of cardiac lesion in rheumatoid arthritis is difficult to assess from the literature but appears to range between 3 and 30 per cent in clinical studies and between 25 and 66 per cent in post mortem studies (Rogen 1947) These figures are probably too high The subject is well reviewed by Bywaters (1950)

PATHOLOGY

In a fulminating attack which ends fatally within two or three weeks tissue microscopy reveals only non specific lesions consisting of œdema fragmentation of collagen leucocytic infiltration hyperæmia and capillary hæmorrhage (Coburn 1933) Similar lesions may occur in most acute infections toxæmias and allergic states and represent the Arthus phenomenon (Werner 1938) Many tissues are so affected particularly the synovial membranes of the larger joints the pericardium myocardium, and endocardium the pleura and lung Petechiæ may be seen clinically in the skin (purpura rheumatica) or in the ocular fundi and at autopsy they are often most obvious in the pericardium and pleura Inflammatory œdema of soft tissues may be seen clinically independent of arthritis Effusion into the large joints and sometimes into the pericardial or pleural cavities is characteristic and is the best example of the exudative type of lesion

The specific rheumatic lesion however is proliferative and occurs rather later it is characterised by the Aschoff node (Aschoff 1904) This is a small collection of large often multinucleated reticulo endothelial cells mixed with lymphocytes and plasma cells surrounding a necrotic collagenous centre there is also fibroblastic proliferation Whilst it is in no sense perivascular it lies in close relationship to a vessel This lesion is particularly well seen in the myocardium Another example of the proliferative lesion is the subcutaneous nodule which may be regarded as an aggregation of Aschoff nodes with fibroblastic tissue predominating (fig 9 01)

Occasionally vascular lesions are found in the viscera which show all the features of panarteritis Involvement of the cerebral pulmonary coronary and mesenteric arteries has been described (Ritchie 1939) Secondary thrombosis may occur but is uncommon Later the media may become calcified

Rheumatic inflammation of the heart valves is a true valvulitis, the baneful agent entering the valve through the minute vessels which supply it (Shaw 1929) There has been considerable disagreement concerning the vascularity of normal and diseased heart valves Langer (1887) first demonstrated the dependence of valvular blood vessels upon the presence of muscle he showed that vessels and muscle fibres reached the free edge of the valve in the fœtus and new born child but soon regressed also th

diseased valves were frequently vascularised whereas normal adult valves were not Gross and Kugel (1921 1925–26 1927–28 1931) who studied the coronary circulation in detail by means of radiography after injecting a barium sulphate gel confirmed Langer s observations They also found that in the fœtus the pulmonary valve was the one best provided with muscle and blood vessels whereas in children it was the aortic cusp of the mitral valve The belief that endocarditis *in utero* usually affected the pulmonary valve whereas in children it usually affected the mitral valve, thus appeared to have a rational basis The decreasing incidence of valvulitis as age advanced was similarly explained More recent work based on the

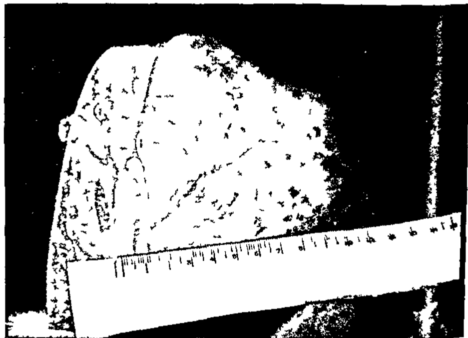


Fig 9 01—Rheumatic nodules in the occipital aponeurosis

injection of Indian ink instead of barium gel however has thrown doubt on these conclusions Wearn *et al* (1936) for instance found capillaries in the valves of 84 per cent of seventy four normal hearts and were unable to correlate the relative incidence of endocarditis of a given valve with the frequency with which it contained blood vessels Thus the mitral valve was vascularised in 66 per cent the tricuspid in 64 per cent the pulmonary in 28 per cent and the aortic in 16 per cent It is possible that the factor governing the relative frequency with which each valve is involved is simply the degree of natural trauma to which each is exposed In a child of 10 for example with a systemic blood pressure of 100/60 mm Hg and a pulmonary blood pressure of 15/5 mm Hg the load supported by the mitral, aortic, tricuspid and pulmonary valves is in the proportion of 100

60 15 and 5 mm Hg respectively According to Cabot (1926) the mitral valve is involved in 85 per cent of cases the aortic in 44 per cent the tricuspid in 10 to 16 per cent and the pulmonary in 1 to 2 per cent which is very close to the relative frequencies that would be predicted if the above hypothesis were correct

In the acute stage of rheumatic inflammation the valve is œdematous and soon shows signs of damage just proximal to its free edge where the cusps come into apposition i e at the site of maximum natural trauma Small thrombi form on the valve at this site giving rise to a ridge or to a row of small pink nodules As the inflammation subsides secondary sclerosis follows and results particularly in fusion of the cusps at the critical areas of tendon insertion (Brock 1952) as described in the next chapter Sclerosis may affect the cusps themselves the chordæ tendineæ the papillary muscles and the mitral ring in varying degree when the damage is slight simple fusion of the cusps (mitral stenosis) is the most likely consequence when the damage is considerable all parts of the valve mechanism become thickened and disorganised and serious mitral incompetence develops According to Carey Coombs (1924) mitral stenosis usually takes 2 to 8 years to develop the stricture increasing very slowly over the years Mitral incompetence usually begins at once during the stage of active inflammation and may progress rapidly in severe cases abetted by dilatation of the mitral ring as the left ventricle dilates in response to its increasing load or as a result of myocarditis once heavy scarring of the mitral valve is well established however the degree of incompetence is unlikely to increase further perhaps rather to the contrary

Fusion of the aortic cusps leading to aortic stenosis also results from secondary sclerosis and usually takes several years to develop the stricture then increasing gradually over the years Aortic incompetence on the other hand like mitral incompetence usually begins during the active stage of the disease, and may progress rapidly in severe cases Slight or moderate leaks may increase gradually over the years as a result of secondary sclerotic changes or if the latter cause increasing fusion of the cusps early incompetence may be replaced by dominant stenosis

CLINICAL FEATURES

In childhood, the heart often bears the brunt of the attack and indeed the joints may escape entirely Once the heart has been involved however carditis or valvulitis should be assumed in all subsequent attacks the increased vascularity of a valve which has been subjected to rheumatic inflammation may partly explain this tendency to recurrence If the first attack occurs over the age of 21 carditis is unlikely and becomes progressively rare with advancing years although it may still occur even in old age Polyarthritis, on the other hand becomes increasingly common

Of 588 rheumatic children studied in detail by Ash (1948), 58 per cent presented first with polyarthritis 8 per cent with subacute rheumatism 19 per cent with chorea, and 15 per cent with isolated rheumatic carditis About one quarter of acute cases have evidence of pre existing rheumatic heart disease when first seen (joint report 1955)

The diagnosis of rheumatic carditis is based on three major issues upon signs of some inflammatory process upon evidence that this process is rheumatic and upon proof of cardiac involvement

SIGNS OF SOME INFLAMMATORY PROCESS

These are fever, leucocytosis and elevation of the erythrocyte sedimentation rate Fever may be of any degree but is usually moderate or high initially in children and moderate or low grade in adults it is irregular in type and inclined to relapse it may last only a few days or it may continue for months The temperature is normal in subacute rheumatism, and may be normal when polyarthritis is still active in acute attacks Leucocytosis is slight to moderate in the early phase of acute rheumatic fever, figures of 10 000 to 15 000 white cells per c mm being the rule The differential count may show a slight relative increase of polymorphs, but is often normal In subacute rheumatism the total count is commonly between 7 000 and 10 000 per c mm The sedimentation rate is by far the most valuable evidence of some active inflammatory process and is often remarkably high when there are no other signs Weekly readings have proved a reliable index of the course of the disease and of the degree of activity In less than 5 per cent of cases the test is valueless the E S R remaining normal throughout the illness

It will be appreciated that these three features are non specific they point to some inflammatory process but they do not determine its nature Secondary anæmia and loss of weight or failure to gain weight may be regarded in a similar light According to Cochran (1951) the normocytic orthochromic anæmia is often apparent rather than real for it may result from hæmodilution the plasma volume being increased as originally observed by Bradley (1938)

EVIDENCE THAT THE INFLAMMATORY PROCESS IS RHEUMATIC

(i) *Polyarthritis* Non suppurative polyarthritis with sterile effusions into the large joints is characteristic Involved joints may be painful swollen hot, flushed and tender on the other hand slight effusion into a knee joint may be detected when there are no other signs or symptoms or the patient may complain of joint pains when there are no signs as in subacute rheumatism The older the patient the more often are the small joints affected and it becomes increasingly difficult to distinguish rheumatic fever from rheumatoid arthritis Pains and effusions tend to flit from joint to joint one recovering as another is involved but not necessarily Occasionally one

knee or other large joint alone is inflamed especially if previously injured and may remain so for weeks or even for months but minimal pains else where may suggest its true nature Other forms of what is thought to be allergic polyarthritis such as the dysenteric variety may be indistinguish able except on other grounds For example dysenteric polyarthritis is pro claimed by associated conjunctivitis and urethritis and by its relation to dysentery

In subacute rheumatism recurrent joint pains occur without effusion and usually without fever or leucocytosis but the sedimentation rate is raised Growing pains confined to the hips knees or ankles mean sub acute rheumatism growing pains described in the muscles ligaments or tendons probably do not (Hawksley 1939)

(2) *Relationship to streptococcal infection* The diagnosis is favoured if the symptoms follow a streptococcal sore throat or some other streptococcal infection, including scarlet fever There is a latent interval of 1 to 3 weeks, usually 10 to 14 days. The significance of this relationship cannot be over stressed It appears to be fundamentally the same as the relationship be tween dysenteric polyarthritis and acute bacillary dysentery or between gonococcal polyarthritis and gonorrhœa Opportunity to study the dysen teric form was afforded by its frequency amongst the troops in North Africa and Italy in the second world war It was characterised by acute poly arthritis involving the large joints by resistance to salicylates by prolonged activity averaging about three months and by associated conjunctivitis and urethritis Joint effusions were sterile and cultures from the conjunctiva and urethra yielded no pathogenic organisms The provocative attack of dysentery was often abortive or very mild and the latent period 10 to 14 days A previous attack of dysentery was invariable and was usually un treated The evidence suggested that a fairly high degree of immunity was necessary for the development of the syndrome Gonococcal polyarthritis was equally common and behaved similarly, except that tenosynovitis re placed conjunctivitis and urethritis was primary The facts suggest that rheumatic fever is streptococcal polyarthritis and bears the same relation ship to the streptococcus as does *dysenteric polyarthritis to the dysentery* bacilli and gonococcal polyarthritis to the gonococcus but instead of con junctivitis urethritis or tenosynovitis there may be carditis chorea, sub cutaneous nodules or marginate erythema

If there is no history of recent sore throat or other streptococcal infection evidence of such may be afforded by an anti streptolysin titre in the region of 200 Todd units High titres do not prove that an illness is rheumatic fever, only that there has been recent hæmolytic streptococcal infection Similar proof may be obtained by finding that the patient s serum aggluti nates an emulsion of hæmolytic streptococci at a titre of 1 200 It is highly *improbable that any case of acute rheumatic fever, whether it be the first* attack or a recurrence will not show such serological changes

A positive test for C reactive protein in the serum provides good

evidence of activity (Anderson and McCarty 1950) but is far from specific in the rheumatic state the abnormal *alpha* globulin that reacts with C polysaccharide being found in a variety of infections necroses and collagen diseases including uncomplicated streptococcal sore throat rheumatoid arthritis and periarteritis

That continued hæmolytic streptococcal infection is not responsible for the disease may be proved by the lack of improvement after treatment with penicillin

(3) *Response to salicylates* Joint pains and effusions in rheumatic fever commonly respond dramatically to sodium salicylate in initial doses of 15 to 20 grains (1 to 1 5 G) aspirin (or calcium aspirin) 5 to 10 grains (0 3 to 0 6 G) three or four hourly Only the exudative lesion and the associated fever respond no effect is observed on proliferative lesions Sodium salicylate is often used as a diagnostic test but although a good one it is not infallible

(4) *Chorea* Rheumatic or Sydenham s chorea is mysterious in several ways First it has a solitary nature preferring to occur alone rather than in the company of other rheumatic manifestations Secondly it does not affect the sedimentation rate Thirdly there is no specific rheumatic pathology in the brain (Shaw 1929) Nevertheless it is certainly part of the rheumatic state About 20 per cent of patients with chorea alone develop rheumatic heart disease about 50 per cent develop other rheumatic manifestations with or without carditis (Sutton and Dodge 1938) and most of the remainder have a familial link Conversely about 20 per cent of all rheumatic cases have chorea (Ash 1948) Clinical features include spontaneous involuntary inco ordinated movements muscular weakness and alteration of tendon jerks emotional instability and some disturbance of higher cortical function Occasionally it is more or less confined to one side of the body Movements disappear during sleep

The diagnosis of chorea must be made from common tics and other forms of hysteria Reliance should be placed on the quality of the movements They are quick complicated elaborate irregular and varied The same movement is rarely repeated exactly The hands writhe and twist the patient trying to stop them or attempting to conceal them by some volitional act She often drops things she is holding especially crockery or she is clumsy in other ways Facial grimaces are odd and varied unlike the repeated twitch of a tic After protruding the tonge for inspection she withdraws it like a lizard snapping the jaws over it When the hands are held out the wrist is flexed and the fingers hyper extended The knee jerk may be sustained, the leg being held up at the height of its extension for an appreciable interval before relaxation occurs

Hysterical movements are more jerky and show constant repetition Experience and familiarity with both conditions usually makes their distinction easy The involuntary athetotic movements of encephalitis and Wilson s disease may be more confusing

5 *Skin lesions* Petechiæ may occur in the skin or in the fundi in fulminating cases but are in no way specific Petechiæ or purpura may be associated with gut colic and joint pains in the Schonlein Henoch syndrome in these cases acute glomerular nephritis is very common rheumatic carditis rare (5 per cent) The syndrome represents another type of allergic *reaction to streptococcal antigen and is related to rheumatic fever* nephritis and polyarteritis (Gairdner 1948) Urticaria erythema nodosum and erythema multiforme are sometimes seen, but they too are not specific They are probably allergic skin reactions and when associated with rheumatic fever may depend upon skin sensitisation to the streptococcus or to its toxins Urticaria may be due to a host of antigens erythema nodosum



FIG 9 02 – Erythema marginatum

to the tubercle bacillus the meningococcus or other organisms erythema multiforme is perhaps more closely related to the streptococcus

Erythema marginatum (Barlow and Warner 1881) a variety of erythema multiforme is especially important because it is peculiar to the rheumatic state (Cheadle 1889) It appears in rings, crescents ovals or in irregular forms, characterised by a thin red margin outlining a patch of apparently normal skin (fig 9 02) It is distributed chiefly over the trunk and proximal part of the limbs There may be two or three lesions or dozens of them Sometimes the rash is at first composed of irregular erythematous macules (fig 9 03) but the centres soon clear leaving spreading red margins (Perry 1937) Erythema marginatum may be fleeting or remarkably persistent as a rule it is recurrent and may reappear from time to time

long after other manifestations of active rheumatism have subsided It is seen in about 8 per cent of cases in the United Kingdom (joint report 1955)

Subcutaneous nodules occur in one fifth of active cases in this country and are good examples of proliferative rheumatic lesions Like erythema marginatum they were first properly studied by Barlow and Warner (1881) although well recognised long previously (Wells 1810) Varying in size from something so small as to escape clinical detection to the dimension of a Barcelona nut they are usually attached to tendon sheaths to the



Fig 9 03—Erythema multiforme

superficial surface of joint capsules or to other fascia so that the skin rides over them freely They are best seen on the knuckles (fig 9 04a) on the back of the head (fig 9 04b) on the elbows or on the knees In children they are practically diagnostic of rheumatic fever, but similar though usually larger and more persistent nodules may occur in Still s disease and in adult rheumatoid arthritis (Hawthorne 1900) It is doubtful whether there is any fundamental difference between these nodules (Keil 1938) In cases of rheumatic fever nodules have been induced artificially by injecting one of a variety of substances including blood trypsin and hyaluronidase into the fibrous tissue or fascia overlying the olecranon process (Massell Coen and Jones 1950)

6 *Pulmonary signs* Because of its non specific clinical features pleurisy rarely provides evidence of rheumatic fever, but it is not uncommon Paul (1928) gave its incidence as 10 per cent It may be dry or it may give



(a) On the knuckles



(b) On the ba k of the head

Fig ›o4 – Subcutaneous rheumat c nodules.

rise to a sterile straw coloured effusion Response to salicylates is indifferent

Rheumatic pneumonia is rare occurring in only 1 to 2 per cent of active cases Symptoms are not spectacular There is no chill, breathing is not embarrassed the respiratory rate is but little elevated, and fever is not necessarily higher than before Cough may be noted, but is rarely troublesome The sputum is scanty and tenacious occasionally it is streaked with blood Physical signs include dullness to percussion bronchial breathing and crepitations appearing first here then there The transient and migratory nature of these signs is characteristic Serial skiagrams confirm the presence of patchy wandering consolidation or may show a variable broncho pneumonic pattern (fig 905) The white blood count is little altered Rheumatic pneumonia is not influenced by penicillin sulphonamides or salicylates fortunately it does not often appear to alter the course of the major illness



Fig 905—Skiagram showing rheumatic pneumonia in a girl

Most cases studied at autopsy have been unusually severe and consolidation has been extensive and mostly lobar in distribution The affected parts are bulky have a peculiar succulent gelatinous appearance (Hadfield 1938) and feel like indiarubber in colour they are a homogeneous rich purplish red (Naish 1928 Eiman and Gouley 1928) and later may be buff Microscopically the predominant finding is an extensive fibrinous exudate infiltrated with mononuclear and multinucleated cells Polymorphs and lymphocytes are scanty The cellular exudate is partly interstitial but also line the alveolar ducts and may fill the alveoli (Hadfield 1938) There is associated hyperæmia and œdema Secondary fibroblastic reaction develops later, and when interstitial may be responsible for pulmonary hypertension (Gouley 1938) Similar lesions have been produced experimentally by Rich and Gregory (1943)

Simple collapse of either lower lobe in the course of rheumatic fever may occur, and must not be confused with rheumatic pneumonia Its cause is obscure, but it may be connected with the long recumbent posture It is seen in many serious illnesses that confine a patient to bed for a long time e g typhoid fever Sometimes collapse of the left lower lobe may be

due to pericardial effusion or to a greatly dilated heart Pulmonary congestion or œdema and infarcts of the lung should be recognised without difficulty

7 *Tolerance to Heparin* Patients with acute rheumatic fever show a remarkable tolerance to heparin and possibly to other sulphated polysaccharides This is at present under investigation and may prove a useful test for the active rheumatic state (Abrahams and Glynn 1949)

EVIDENCE OF CARDITIS

To establish the diagnosis of rheumatic carditis at least one of its five chief manifestations must be recognised It should be clearly understood that while these offer proof of cardiac involvement they do not by themselves necessarily signify a rheumatic etiology—that must be demonstrated in other ways

1 *Mitral valvitis*

1 The development of a *mitral pan systolic murmur* embracing both heart sounds at the apical area must be taken seriously Towards the end of the nineteenth century apical systolic murmurs of all kinds were attributed to mitral valve disease and patients were put to bed for long periods unnecessarily to combat this tendency Mackenzie taught that the apical systolic murmur could be safely disregarded when unaccompanied by other signs of heart disease and this teaching was perpetuated and emphasised by Lewis and Parkinson As a result the original diagnostic fault has been over corrected and it is becoming increasingly obvious that an important murmur is not receiving proper attention The confusion has been caused partly by *failure to distinguish the pan systolic murmur of* mitral incompetence from the relatively short mid systolic aortic ejection murmur transmitted to the apex The latter is often innocent as explained elsewhere but the mitral pan systolic murmur means mitral incompetence and nothing else and it is high time this indisputable fact was more widely recognised The mitral murmur of course must be distinguished from the pan systolic murmur of ventricular septal defect and tricuspid incompetence both of which may be heard best sometimes at the apex of the heart but if the apical murmur is mitral then the only diagnostic problem is whether the mitral incompetence is functional, secondary to ring dilatation or organic resulting from a diseased mitral valve Functional mitral incompetence means left ventricular dilatation just as functional tricuspid incompetence means right ventricular dilatation and both are important for dilatation of either ventricle cannot be viewed with equanimity In rheumatic carditis for example functional mitral incompetence usually means serious aortic incompetence with or without left ventricular failure and is far more important than trivial mitral valvulitis to which an isolated mitral pan systolic murmur should be ordinarily attributed

In quality the mitral pan systolic murmur is usually loud smooth and blowing being of fairly high frequency it is better heard with the diaphragm type of chest piece A thrill is uncommon in the early stage of active inflammation and when it occurs usually means considerable permanent damage to the valve Follow up studies have shown that chronic rheumatic heart disease develops in 45 per cent of cases in which the original murmur was loud and in only 9 per cent of those in which it was soft (Boone and Levine 1938 Kuttner and Markowitz 1948)

Other evidence of significant mitral incompetence includes a small slightly water hammer pulse, an otherwise unexplained rise of venous pressure a hyperdynamic enlarged left ventricle (clinically electrocardiographically and radiologically) a loud third heart sound and radiological evidence of dilatation of the left atrium with or without pulmonary venous congestion When valvitis is severe, permanent incompetence may be established within a few weeks of the onset of rheumatic carditis

The development of a *soft short mitral diastolic murmur* (Carey Coombs murmur) in the absence of any other sign of mitral stenosis provides by far the most useful and conclusive evidence of mitral valvitis At the rheumatic fever centre Taplow this murmur has been heard in 75 to 80 per cent of active cases Although transient in 20 to 25 per cent it usually proves to be more or less persistent or reappears on the least provocation until pre systolic accentuation and a loud first heart sound proclaim the development of mitral stenosis (Carey Coombs 1924)

This characteristic and diagnostic murmur is frequently overlooked because it is very low pitched soft and short it is best heard with the bell stethoscope when the patient lies on the left side especially as the heart slows down after effort and has the typical mid diastolic timing of all mitral diastolic murmurs We thought at Taplow that the murmur could be brought out or accentuated by any agent that increased the mitral stroke blood flow and that phenylephrine (neosynephrine) was perhaps the best way of achieving this When given in doses of 0 25 mg intravenously the blood pressure rises sharply and the murmur develops as the heart slows down (Besterman 1951)

Necropsies have confirmed the fact that this murmur may occur in active rheumatic carditis when the mitral valve is scarcely altered (Bland White and Jones 1935) It has therefore been suggested that its mechanism depends upon left ventricular dilatation that it is related to the Austin Flint murmur and to the soft mitral diastolic murmur that is occasionally heard in thyrotoxic heart failure But it must be pointed out that the Carey Coombs murmur is usually heard when no enlargement of the heart can be demonstrated and it is more reasonable to believe that some change in the structure of the mitral valve is responsible Whatever the explanation there is no doubt that this murmur occurs early in the course of rheumatic carditis and may disappear as activity subsides

2 *Aortic valvitis*

Inflammation of the aortic valve usually leads to immediate and permanent aortic incompetence which may be recognised at once by the tell tale aortic diastolic murmur The initial leak is small so that other evidence is usually lacking When first heard the murmur may be remarkably short and high pitched and its onset is slightly delayed being inaudible until the diastolic pressure gradient across the aortic valve is approaching its maximum i e towards the end of the period of isometric relaxation when the left ventricular pressure is approaching zero The triple rhythm cadence so produced may be disconcerting to the student who is only familiar with the to and fro murmurs of well established aortic valve disease but it is characteristic of these early cases

An aortic diastolic murmur was heard in 45 per cent of cases at Taplow and one in five was transient Phenylephrine was again helpful in accentuating the murmur or bringing it out when it could not otherwise be heard for the temporarily raised blood pressure and increased stroke volume encouraged the leak (Besterman 1951)

An isolated aortic mid systolic ejection murmur heard best at apex or base provides insufficient evidence of aortic valvitis to warrant a diagnosis of active rheumatic carditis for it is too commonly produced by a simple increase of blood flow associated with any fever or as a result of other innocent phenomena such as a depressed sternum A functional basal systolic bruit may also be pulmonary rather than aortic and this too is usually a functional flow murmur turbulence being created by a variety of innocent causes

3 *Partial heart block*

Transient prolongation of the P R interval (fig 9 06) is recorded in about 10 per cent of cases but may well be more frequent than this It may be recognised clinically by premature *a* waves in the jugular venous pulse occasionally by regular venous cannon waves when P falls between the onset of QRS and the end of the T wave of the previous cycle, by pre maturepre systolicgallop rhythm the interval between pre systolic and first heart sounds being prolonged and by softening of the first heart sound the atrioventricular valve cusps *floating* into apposition after atrial contraction is completed so that the atrioventricular valves are already more or less



Fig 9 06—Electrocardiogram showing prolongation of the P R interval in a case of active rheumatic carditis

closed when the ventricles contract Dropped beats are unusual and more severe grades of heart block rare Normal conduction can be temporarily restored in 90 per cent of cases by means of 1 to 2 mg of atropine sulphate intravenously (Bruenn, 1937) Some degree of permanent block is likely in those that do not respond to atropine

4 *Pericarditis*

Rheumatic pericarditis occurs in about 10 per cent of cases it is always acute commonly develops during the first month of the illness and leaves no clinical sequelæ In mild cases there is little more than transient pericardial friction with or without pain Most cases that are recognised however are relatively severe and the inflammation is accompanied by considerable pain high fever rapid breathing and obvious distress there is usually leucocytosis and the sedimentation rate is always high A rise of venous pressure and proportionate distension of the liver are usual, for fluid tends to accumulate rapidly dangerous tamponade however is rare and therapeutic tapping nearly always unnecessary The electrocardiogram may show characteristic early elevation of the S T segment followed by flattening or slight inversion of the T waves in most leads as in other forms of pericarditis (fig 9 07) but these changes are found in only a little over half the cases and are rarely very conspicuous Rapid changes in the size of the heart shadow provide the most reliable radiological evidence of pericardial effusion (fig 9 08) changes in shape being less important Samples of the fluid are straw coloured, sterile and have the physical properties of an exudate

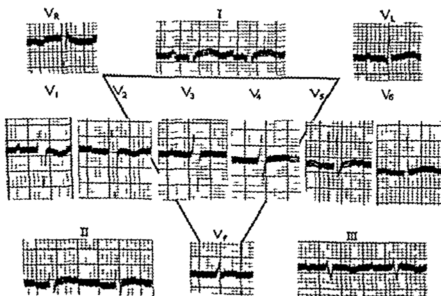
Pericardial effusion is the usual cause of apparent cardiac enlargement in rheumatic carditis in the absence of serious valve damage or heart failure (Wood 1950 Thomas Besterman and Hollman 1953)

5 *Heart failure*

Investigations on cardiac function in rheumatic carditis carried out at Taplow seemed to establish three things (1) in cases uncomplicated by gross valve damage pericardial effusion or congestive heart failure tachycardia is not disproportionate to fever and anxiety and the relationship between cardiac output and heart rate does not differ from that in normal controls (Hollman 1950) (2) cardiac dilatation rarely if ever occurs in simple rheumatic carditis enlargement of the heart shadow nearly always being caused by serious permanent valve damage, pericardial effusion or congestive failure (Wood 1950 Besterman and Thomas 1953) (3) the resting cardiac output in uncomplicated cases is probably normal but the maximum output is strictly limited and frequently reached as a result of anxiety alone (Besterman 1954) There is no simple bedside way of demonstrating this impairment of cardiac function

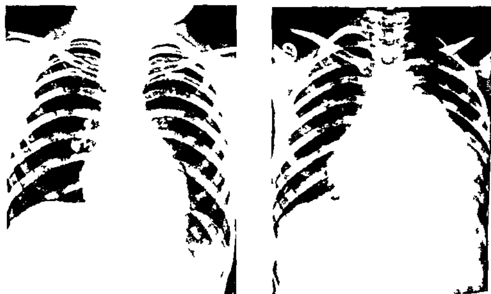
Congestive heart failure proper with elevation of the venous pressure distension of the liver and a fall in cardiac output, with or without œdema or ascites is rare in the absence of advanced aortic or mitral valve disease

(a) Early stage with elevation of the S T segment



(b) Three days later with flattened T waves

Fig. [illegible] — The electrocardiogram in rheumatic pericarditis



(a) 24th November 1947 (b) 1st December 1947

Fig 9 08—Rapid change in the size of the heart shadow in a case of pericardial effusion

its development during the course of rheumatic fever provides good evidence of active carditis

The chief clinical difficulty is to distinguish heart failure from pericardial effusion The points favouring effusion have already been enumerated *The distinguishing features of heart failure include (1) the relatively late* onset of the episode in question the signs suggesting heart failure rarely appearing within the first three months of the illness (2) the presence of advanced aortic or mitral valve disease usually incompetence (3) a low or falling sedimentation rate absence of leucocytosis and a normal or subnormal temperature (4) œdema or ascites (5) a relatively fixed degree of cardiac enlargement (6) radiological evidence of pulmonary venous congestion but no pleural effusion (7) a good response to digitalis therapy (Thomas 1954)

Despite these numerous points of difference the distinction between acute pericarditis with effusion and heart failure may be difficult at times Figure 9 09, for example illustrates the rapid development of cardiac dilatation from heart failure The first skiagram (a) was taken on the 23rd March 1948 in a quiescent phase one week before a recurrence of rheumatic fever at a time when the temperature was normal the E S R 18 and the only evidence of carditis a Carey Coombs murmur The second skiagram (b) was obtained six weeks later on the 8th May one week before death, and shows gross dilatation of the heart shadow at a time when the patient s temperature was 102 degrees F the sedimentation rate 56 and pericardial friction widespread At necropsy there was only 20 ml of fluid



(a) 23rd March 1948 (b) 8th May 1948

Fig 9 09—Unusually rapid change in the size of the heart shadow in a case of heart failure (see text)

in the pericardial sac and the enlargement was caused chiefly by dilatation of the left ventricle as a result of heart failure secondary to rheumatic carditis in the presence of advanced aortic and mitral valve disease The pericardium however was considerably thickened

The only way we were able to establish the criteria for distinguishing between cardiac dilatation and pericardial effusion was by proving which was present by means of cardiac catheterisation (fig 4 57)

Other manifestations of carditis

It is doubted if there are any other manifestations of rheumatic carditis *Sinus tachycardia* is not disproportionate to fever anxiety pericardial effusion or heart failure *Gallop rhythm* in a child is difficult to distinguish from a normal third heart sound *Enlargement of the heart shadow* rarely if ever occurs in the absence of advanced valve disease heart failure or pericardial effusion

The *electrocardiogram* shows no obvious changes other than those depicting partial heart block pericarditis or the consequences of advanced valve disease

Prolongation of the Q T interval was found by Taran and Szilagyi (1947) in practically all cases of active carditis and this has been confirmed apparently by Abrahams (1949) In fig 9 10 the corrected Q T interval (Q T) in sixty cases of active carditis and fourteen cases of rheumatic fever without carditis has been plotted against the sedimentation rate on a semi logarithmic scale It will be seen that about 90 per cent of those with

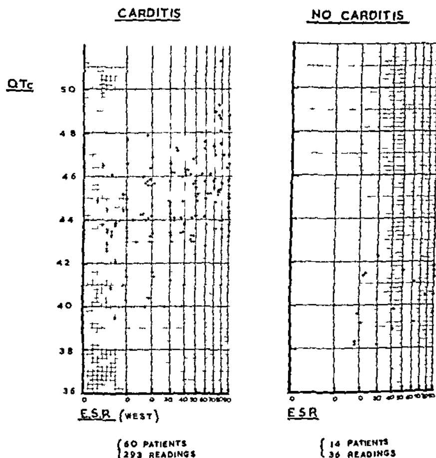


Fig 9 10—Graph showing QT plotted against the sedimentation rate in 60 ca es of active rheumatic carditis and in 14 rheumatic fever controls without carditis
(By ou t y f D D k Ab ah; s)

carditis have a QT longer than 0 42 second whereas all but one of those without carditis fall below this level Fig 9 11 shows the behaviour of QT in six typical cases of acute rheumatic carditis with rapid recovery In fig 9 12 a relapse is portrayed it may be observed that QT then remains grossly prolonged although the sedimentation rate is falling towards normal If the long QT_c is ignored and the patient is allowed up relapse may occur It must be stated however that further detailed work on the behaviour of QT_c in rheumatic carditis has thrown considerable doubt on its value

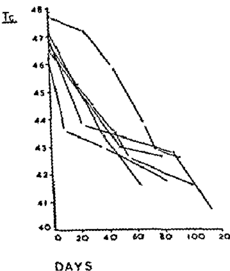


Fig. 9.11—Behaviour of QT in six cases of acute rheumatic carditis with rapid clinical recovery

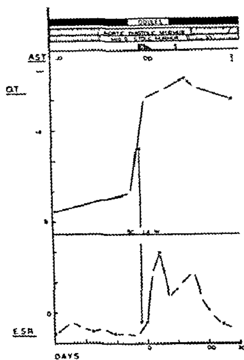


Fig. 9.12—Prolonged QT following a recurrence of active rheumatic carditis

(By courtesy of Dr Derek Abrahams)

TREATMENT

All cases of acute or subacute rheumatic polyarthritis should be put to bed and treated with sodium salicylate, 15 to 20 grains (1 to 1.5 G), combined or not with twice as much sodium bicarbonate three hourly (Lees 1904) until relieved or until ringing in the ears and deafness proclaim that the desired therapeutic salicylate blood level of 30 to 35 mg per cent has been reached when the interval between doses may be increased to four or six hours. Aspirin or calcium aspirin, 10 gr. (0.6 G.), is equally effective. Fever pain and joint effusions usually subside quickly but proliferative lesions including carditis are resistant. Toxic effects are minimised by alkalis: this has been attributed to an increased rate of salicylate excretion in their presence (Parker 1947, 1948). Toxic effects include central vomiting, hyperventilation associated with an increased oxygen consumption (Cochran 1952) and which sometimes results in reduction of the plasma CO_2 content (Graham and Parker 1948) and petechiae associated with prolongation of the prothrombin time (Link et al., 1943). Fatal hæmorrhagic encephalopathy has been reported (Ashworth

and McKemie, 1944) Circulating prothrombin can usually be restored by means of vitamin K in doses of 10 to 50 mg (Shapiro 1944)

When the patient has been free from symptoms for a week or if he fails to derive benefit salicylates should be stopped If clinical relapse follows no harm is done for the exudative lesion is relatively innocent, and is soon controlled by another course

Salicylates were introduced by Bliss (1875) and Maclagan (1876) and their action is still uncertain It was suggested long ago that they might inhibit antibody formation (Derick Hitchcock and Swift 1927–8) a conception that received some support from Jager and Nickerson (1947) who showed that salicylates reduced the amount of H and O antigens produced in response to typhoid vaccine Salicylates increase the plasma volume (York and Fischer 1947) there being a profound shift in the distribution of body fluid from intracellular to extracellular compartments (Reid Watson and Sproull 1950) Following this line of thought Copeman and Pugh (1950) reported rapid clinical improvement in 7 cases of acute rheumatic fever following an injection of hypertonic saline the patients having been dehydrated previously by means of food and fluid starvation for 36 hours Another way in which salicylates may influence the symptoms of rheumatic fever is by inhibiting hyaluronidase (Guerra 1946) This enzyme hydrolyses hyaluronic acid a polysaccharide present in mucoprotein which is a constituent of the ground substance of all connective tissue (Chain and Duthie 1939) The effect of this is to increase the rapidity with which substances spread through collagen as may be demonstrated by measuring the rate of spread of a suitable dye when injected intradermally In rheumatic fever injected dye spreads more rapidly than in normal controls as if an excess of hyaluronidase were present (Guerra 1946) and serum from patients with active rheumatic fever has been shown to contain an excess of anti hyaluronidase (Quinn 1948) Whether the hyaluronidase factor in rheumatic fever depends on the power of the culpable streptococcus to produce it or whether it arises from some other source is immaterial in respect of the action of salicylates, although possibly fundamental in relation to the cause of rheumatic fever itself Another effect of salicylates is to reduce the permeability of damaged capillaries (Swyer 1948) and this should certainly limit the exudative reaction Yet another hypothesis is that salicylates have an action like A C T H for Hetzel and Hine (1951) have shown that therapeutic doses of salicylates diminish the ascorbic acid content of the suprarenal glands in rats (generally regarded as evidence of increased cortical activity) the effect being abolished by hypophysectomy Van Cauwenberge (1951) found a reduction of circulating eosinophils in rats four to six hours after the ingestion of salicylates preceded by a significant increase of the urinary uric acid/creatinine ratio both of which have been attributed to increased activity of the suprarenal cortex Finally, it must be remembered that a break down product of sodium salicylate may well be responsible for its

therapeutic effects rather than the drug itself and in gentisic acid we have a metabolite that seems to fulfil these expectations sodium gentisate in doses of 1 G three hourly relieves the symptoms of rheumatic fever as quickly and completely as salicylates and has the advantage of minimal toxic effects (Meyer and Ragan 1948 Clarke 1953)

Recent work at the Mayo Clinic on the beneficial effect of cortisone (17 hydroxy 11 dehydrocorticosterone) on rheumatoid arthritis (Hench *et al* 1949) provided a new approach to the treatment of rheumatic states in general but initial enthusiasm has already abated and in rheumatic fever both cortisone and A C T H have been shown to be no more effective than aspirin (Joint report 1955) The usual dose of cortisone is 200 mg daily for the first week 100 mg daily for the second and third weeks and 75 to 25 mg thereafter the daily dose being reduced by 25 mg at weekly intervals and the total course lasting six weeks Cortisone may be given intramuscularly or by mouth A C T H (adreno cortico trophic hormone or corticotropin) is given intramuscularly in daily doses of 100 units for the first week 80 units for the second 60 units for the third 40 for the fourth 30 for the fifth and 20 for the sixth

Both cortisone and corticotropin like aspirin relieve fever and joint pains quickly in rheumatic fever and the sedimentation rate falls in a gratifying manner but myocarditis endocarditis pericarditis nodules erythema marginatum and chorea do not seem to be influenced by any of these substances

Neither sulphonamides nor penicillin have any influence on the course of rheumatic fever if given after the onset of rheumatic symptoms but both are valuable prophylactic agents Sulphadiazine in doses of 0 5 G once or twice daily oral penicillin or benzathine penicillin in doses of 200 000 to 500 000 units daily or monthly intramuscular injections of 1 to 1 5 mega units of benzathine penicillin, all greatly reduce the frequency with which group A hæmolytic streptococci can be cultured from the throats of rheumatic children or carriers and reduce the frequency of recurrencies (Stollerman Rusoff and Hirschfeld 1954 Perry and Gillespie 1954) Unfortunately intramuscular benzathine penicillin is often very painful There is also good evidence that penicillin lessens the chances of the rheumatic reaction if given early enough to cases of group A hæmolytic streptococcal sore throat (Rammelkamp 1952) and this may be supported by the demonstration that penicillin therapy suppresses antibody formation as judged by the anti streptolysin titre and that the sooner penicillin is given in cases of tonsillitis the greater the suppression of antibody (Brock and Siegel 1953)

Tonsillectomy is only necessary if there is chronic sepsis or if there is recurrent tonsillitis it has little influence on the disease and does not prevent relapse or recurrence (Ash 1938) A good nourishing diet fresh air vitamins especially vitamin C appropriate treatment of secondary anæmia and high morale are more important

Chorea usually lasts 6 to 12 weeks Patients should be put to bed during the active phase, and may need heavy sedation If there is no evidence of carditis they may be allowed up when recovery begins They should be kept away from school and from social engagements until well

Carditis requires absolute rest Little else is of lasting value Digitalis is helpful when there is congestive heart failure and although the thera peutic dose is said to be close to the toxic ill effects have not been observed at Taplow Mercurial diuretics and a low sodium diet are rarely necessary

Absolute rest means that the patient is allowed to do nothing for himself he is washed and fed and must use bed pan and urine bottle Diet should be light and constipation avoided In the past it was usual to insist on nursing the patient in the horizontal position with one low pillow but it is clear from experience gained in the treatment of angina decubitus and of paroxysmal cardiac dyspnœa and from certain direct investigations in man that the cardiac output and therefore the work of the heart, is greater in the horizontal than in the upright position owing to the influence of gravity on the venous *filling pressure It is therefore logical to nurse* patients with carditis in the sitting posture The wisest course may be to chose the position of maximum comfort whether lying or sitting unless there is failure when the latter should be insisted upon

By far the best index of activity is the E S R , which should be measured weekly and as a rule the patient should not be allowed up until it is normal. This applies especially to children in whom carditis should be assumed *for purposes of early management* Adults without evidence of previous or pre sent carditis may be treated more leniently and may be allowed up as soon as they appear well enough on clinical grounds The duration of bed rest varies between a week or two and several months according to the severity and persistence of the active process If patients are allowed up too soon swift relapse is the rule

Convalescence from carditis should be extended over several months the regime being similar to that for pulmonary tuberculosis Relapse is common and may be due to over exertion exposure, emotional upset, cold damp weather, and to almost any infection Relapse follows the advent of the responsible agent immediately and must be distinguished from a recur rence or second attack of rheumatic fever in which streptococcal *infection* is always to blame and following which a latent interval can usually be recognised At least one recurrence occurs in two thirds of all cases usually within three years (Roth Lingg and Whittemore 1937)

It is as important to prevent cardiac neurosis in patients with organic heart disease as it is in those without This is a difficult task in susceptible individuals for reassurance cannot very well be unconditional Rheumatic carditis may be symptom free and pass without influencing the subject's activities at all Thus only about 55 per cent of cases of mitral stenosis give a history of the original attack (Parkinson and Hartley 1946) Many others are only restricted by subacute rheumatism Little immediate harm comes

to these patients indeed there is no direct evidence that subsequent development of mitral stenosis could have been prevented by bed rest at the time of active inflammation It follows that failure to diagnose carditis when it is present in rheumatic fever is not necessarily disastrous On the other hand its diagnosis in error may not be far short of it for the resulting cardiac neurosis which is so common may be life long and may be more incapacitating than organic heart disease Physicians should be more aware of their responsibility in this respect Too much emphasis is laid on overlooking a mild lesion not enough on finding what is not there The most common mistake is to misinterpret tachycardia A patient confined strictly to bed for several weeks with rheumatic fever is fully aware that his heart may be involved and is likely to become nervous on that account Tachycardia may then be due to anxiety Again, the autonomic nervous system is frequently disturbed by fever and infections of all kinds tachycardia dizziness, headache and fatigue may result especially during convalescence when activities are resumed Such findings call for reassurance and rehabilitation not for alarm and further rest

In the absence of diagnostic evidence of carditis throughout the active phase of rheumatic fever subsequent medical management should be based on the assumption that none existed not upon the fear that it escaped recognition and patients should be sent for convalescence as after any other fever of equal severity This attitude is based not on the belief that carditis does not occur in a certain percentage of children with rheumatic fever but on the fact that if it does occur in an indetectable degree it is either of no consequence or it is not aggravated by this kind of management and on the fact that the over cautious attitude breeds neurosis

COURSE AND PROGNOSIS

Following convalescence from rheumatic fever between 60 and 65 per cent of cases have evidence of residual valve damage but 10 to 20 years later 9 to 16 per cent of these seem to have recovered completely on the other hand 23 to 44 per cent of those who appear to escape unscathed develop signs of chronic rheumatic heart disease within the same 10 to 20 year period (Ash 1948 Bland and Jones 1951) The net result is that at least two thirds of all cases of rheumatic fever in childhood develop permanent valve damage

Rheumatic carditis is more likely to be associated with polyarthritis (61 per cent) than with subacute rheumatism (38 per cent) or chorea (20 per cent) Isolated carditis however must occur much more frequently than its 15 per cent incidence would imply because 40 per cent of all cases of chronic rheumatic heart disease in adults give no history of any rheumatic manifestations in childhood Allowing for this it is estimated that one third of all rheumatic cases in childhood have isolated carditis and that two thirds of these are overlooked at the time No previously published

figures concerning early mortality and ultimate prognosis have allowed for these silent cases of primary carditis For example according to Ash (1948) about 48 per cent of cases presenting with primary carditis in childhood die within 10 years but these of course are the cases that are recognised because of their severity and isolated rheumatic carditis must be severe to cause symptoms If allowance is made for the relatively mild unrecognised cases practically none of which die within 10 years Ash s figure changes from 48 to 16 per cent

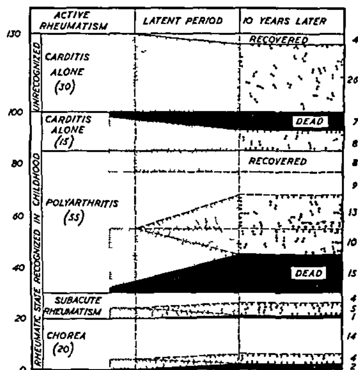
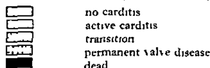


Fig 9 13—Chart depicting the course of the rheumatic state over the first ten years (modified from figures published by Rachel Ash 1948)



In figure 9 13 an attempt has been made to chart the course of rheumatic fever over the first 10 years based on the papers by Ash (1948) and Bland and Jones (1951) but modified so as to allow for the unrecognised cases Taking into consideration the known data it may be calculated that to every 100 recognised cases of juvenile rheumatism with or without carditis there must be an additional 30 cases of unrecognised pure rheumatic carditis assuming that between 10 and 15 per cent of the latter recover

completely as in the recognised cases of carditis The chart shows that 10 years after the onset of the rheumatic state 25 out of 130 cases are dead (19 per cent) 66 (51 per cent) have chronic rheumatic heart disease and 39 have recovered completely (30 per cent) It also shows that of the 66 living cases with permanent valve damage 26 (40 per cent) were not recognised during the stage of active carditis The relatively good prognosis of subacute rheumatism and chorea will not escape notice

Of the fatal cases one third die within one year of the onset of rheumatic carditis and two thirds (Bland and Jones 1938) to three quarters (Ash 1948) within the first five years Thus the immediate mortality is 6 5 per cent as reported by Scott (1943) Sudden unexpected death is rare in contrast to its frequency in diphtheritic and certain other forms of toxic myocarditis thus there were only three such instances amongst a group of 7 165 cases of active rheumatic fever reported by Griffith and Huntington (1946) coronary angiitis was blamed

The prognosis is of course greatly influenced by the severity of the active state Thus in a 20 year follow up study of 1 000 cases Bland and Jones (1951) found that 80 per cent of those who had developed heart failure 63 per cent of those with pericarditis and 37 per cent of those with nodules had died

Recurrences or relapses are the rule rather than the exception 40 per cent of cases having a second attack within 2 years 58 per cent within 5 years and 63 per cent within 10 years (Ash, 1948) Thus two thirds of recurrences might be prevented by adequate antibiotic therapy for a period of two years after the initial attack

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CHAPTER X

CHRONIC RHEUMATIC HEART DISEASE

RHEUMATIC carditis refers to active inflammation of the heart The after effects which include valve sclerosis patchy myocardial fibrosis, and adherent pericardium are best described under the general heading of rheumatic heart disease to which the appropriate anatomical abnormality may be appended Thus we may speak of rheumatic heart disease with mitral stenosis

About 5 per cent of healthy young adults give a previous history of rheumatic fever in childhood (Parkinson and Hartley 1946) It is clear therefore that all patients who have rheumatic fever do not later develop clinical rheumatic heart disease According to Carey Coombs (1924) 50 per cent of children who have their first attack of rheumatic fever before they are five years old and 25 per cent of those whose first attack occurs after the age of ten subsequently develop rheumatic heart disease As described in the last chapter recent studies indicate that more accurate figures for these two groups would be 75 and 50 per cent respectively The frequency of permanent valve damage from primary rheumatic fever after the age of 20 does not seem to be known but is far from negligible

From large samples of the younger male population of Great Britain examined for military service between 1939 and 1945 it was calculated that there were about 240 000 cases of rheumatic heart disease of both sexes between the ages of 18 and 44 in Great Britain at that time or about 2 6 per c nt of the population in that age group (Parkinson 1945) Rheumatic heart disease accounts for approximately 20 per cent of all cases of heart disease in temperate climates and causes about 10 000 deaths annually in Great Britain

Practically all clinical cases of inactive rheumatic heart disease have one or more valve lesions The mitral valve is involved in 85 per cent, the *aortic in 44 per cent the tricuspid in 10 to 16 per cent, and the pulmonary in 1 to 2 per cent (Cabot 1926)* The relative frequency with which each valve is affected is proportional to the pressure load against which each normally operates

The rheumatic process affects the heart muscle as well as the valves and this may result in a varying degree of permanent interstitial myocardial fibrosis. Moreover, *it has long been known that careful microscopy reveals Aschoff nodes in all stages of development maturity and senescence in about 50 per cent of all fatal cases of chronic rheumatic heart disease the figure being higher in those that die under the age of 40 years than in* older patients (de la Chapelle Graefe and Rottino 1934 Werner 1936)

The more recent frequent discovery of Aschoff nodes in left atrial appendicular biopsies in 45 to 50 per cent of cases of mitral stenosis treated by valvotomy (Decker *et al* 1953 McKeown 1953) should have caused no surprise and merely confirms what was already well established Although there is usually no other pathological or clinical evidence of activity in these cases there is no valid reason for doubting that these Aschoff nodes represent continually relapsing or chronic active carditis Although the myocardial lesion is certainly less important than the valve damage in at least 95 per cent of cases it cannot be ignored

Rheumatic pericarditis leaves no clinical sequelæ Although the pericardium may become adherent to surrounding structures or its two layers fused and thickened such changes do not seem to interfere with cardiac function Chronic constrictive pericarditis is never rheumatic For the most part then chronic rheumatic heart disease is mitral aortic or tricuspid valve disease or any combination of these three lesions together with their complications its course may be modified but very rarely determined by relapsing or chronic myocarditis or by the degree of myocardial fibrosis present

MITRAL INCOMPETENCE

In the last century this was the most common valve lesion diagnosed Owing to the exertions of Mackenzie Lewis Parkinson and others the first half of the twentieth century witnessed a diagnostic revolution so that a physician who asserted that a patient had organic mitral incompetence had to be very sure of his grounds The change in outlook saved a host of normal subjects from invalidism But the pendulum swung much too far and serious efforts were being made to correct this tendency when the introduction of mitral valve surgery in 1948 forced the pace so that in a short space of time the whole subject received the concentrated attention of investigators all over the world and mitral incompetence was quickly seen in its proper perspective

INCIDENCE

In an unselected series of 300 cases of mitral valve disease studied in detail by the author mitral incompetence was the major hæmodynamic fault in 34 per cent (Wood 1954) About half of these cases had no obstructive stenosis and the other half had mixed stenosis and incompetence with the latter dominant *Mild incompetence complicating* dominant stenosis will be considered later This means that in rheumatic heart disease mitral incompetence is the main valve lesion more often than aortic stenosis or aortic incompetence but not as often as aortic valve disease as a whole Approximately 70 per cent of the cases were serious and would have been treated surgically had there been a satisfactory valve repair operation to offer

AGE AND SEX

The average age of the patients with mitral incompetence was 37 2 which was the same as the average age of the patients with mitral stenosis

The sex ratio is 3 2 in favour of males in cases of pure mitral incompetence and 1 1 in mixed cases in which incompetence is at least as important as the stenosis

PATHOLOGY

As emphasised by Brock (1952) serious mitral incompetence means greater disorganisation of the mitral valve mechanism than that found in simple mitral stenosis and implies a more vicious form of active endocarditis in the first instance a view supported by the previous history actually obtained (Wood 1954)

The most important causes of mitral incompetence are shortening of the valve cusps so that they cannot meet in systole and shortening of the musculo tendinous control the papillary muscles and *chordæ tendinæ* being shortened matted and densely adherent to the valve so that the latter cannot close Brock (1952) graphically described the situation as a fibrous ankylosis of the valve mechanism the two chief causes cited being commonly found together Heavy calcification is not infrequently associated and adds to the rigidity of the system although its very exuberance may diminish the size of the orifice

Mitral ring dilatation is a relatively rare cause of incompetence in chronic rheumatic heart disease in these cases the orifice is very large and although the cusps may be short and thick there is less fibrous rigidity than in the type previously described Early left ventricular failure with ring dilatation during the stage of active carditis may be responsible

HÆMODYNAMICS

During systolic the blood that leaks back into the left atrium increases the volume of that chamber and the pressure within it When the left ventricle relaxes in diastole it is subjected to the high filling pressure built up in the left atrium during systole and since there is no real obstruction at the mitral orifice it fills rapidly and dilates to accommodate the extra blood that leaked back during the previous cycle The stroke volume of the left ventricle is therefore increased by the amount of regurgitant blood forward flow being maintained as near to normal as possible although falling short of the ideal in all serious cases In the majority of cases with fibrous ankylosis of the mitral valve left ventricular dilatation is unlikely to exert any influence on the mitral ring or size of the orifice a vicious circle mechanism however is easily established in active rheumatic carditis and in functional mitral incompetence secondary to left ventricular failure from other causes

Although the left atrial pressure may be very high during ventricular

systole, it falls quickly to ventricular level in diastole so that mean left atrial and pulmonary artery pressures are lower than in mitral stenosis of comparable severity Short of left ventricular failure the patient with mitral incompetence is also less embarrassed by tachycardia or sudden increases of right ventricular output than his sister with mitral stenosis for a shortened diastole does not prevent proper ventricular filling and the hyperdynamic left ventricle may have sufficient reserve to deal with an increased flow Moreover, peripheral vasodilatation on effort encourages forward flow

The pulmonary vascular resistance may rise moderately in severe mitral incompetence but rarely reaches extreme levels probably because passive pulmonary hypertension is rarely high enough to excite a vasoconstrictor response

CLINICAL FEATURES

Life history

Organic mitral incompetence severe enough to shape the medical destiny of the patient is usually well established during the stage of active carditis unlike mitral stenosis its detection demands no latent interval Subsequent sclerosis of valve cusps and chordæ may modify the leak but as a rule there is little basic change in the physiology of the situation over the years until left ventricular failure sets in or reactive pulmonary hypertension alters the course of events The date of the initial inflammation and the average age of death are much the same as in mitral stenosis (q v) but the symptom free period is a little longer and the downhill course once symptoms have started is a little quicker in mitral incompetence (5 3 years to reach total incapacity against 7 3 years in mitral stenosis)

Symptoms

The symptoms of pure mitral incompetence are usually less spectacular than those of mitral stenosis Acute pulmonary œdema, for example is eight times less common, presumably because the mean left atrial pressure is rarely so high as in mitral stenosis of comparable severity and does not rise so sharply on effort or as a result of tachycardia Hæmoptysis is half as common as in mitral stenosis no doubt for the same reason Angina pectoris is also only half as common despite the increased work undertaken by the left ventricle this may be attributed to the rarity of an extreme pulmonary vascular resistance so that forward flow and therefore coronary filling are not hindered by this additional factor Systemic embolism is at least one and a half times less frequent than in mitral stenosis probably because there is less stasis in the left atrium

In mixed cases in which it is uncertain whether stenosis or incompetence is dominant even after elaborate investigation and even digital examination of the valve both hæmoptysis and systemic embolism are at least as common as they are in mitral stenosis perhaps more so The mean left atrial

pressure is higher in these cases then in pure incompetence and there is more stasis to encourage thrombosis in the conspicuously dilated left atrium

According to Brigden and Leatham (1953) the only special symptom of mitral incompetence is palpitation and they ascribe this to the frequency of ectopic beats The hyperdynamic action of the left ventricle, however may also contribute to this symptom

Effort intolerance is usually due to dyspnœa caused by pulmonary venous congestion as in mitral stenosis but sooner or later left ventricular failure adds its own contribution Some protection may be afforded by the rapid dilatation of the left ventricle early in diastole so that the inter ventricular septum bulges into the cavity of the right ventricle, and interferes with proper filling of that chamber (Bernheim effect) Congestive failure usually occurs without a high pulmonary vascular resistance the œdema being due to the poor renal blood flow secondary to the low output, and the raised venous pressure partly to hydræmia and perhaps partly to a Bernheim effect The left ventricle is certainly over loaded but the right may very well not be This behaviour is radically different from the congestive failure of mitral stenosis for which a high pulmonary vascular resistance or uncontrolled atrial fibrillation is nearly always chiefly responsible



Fig 10 01 —Direct brachial arteriogram from a case of mitral incompetence showing an abrupt percussion wave ill sustained peak and late systolic collapse

Physical signs

The patient is usually a man and may look well Peripheral cyanosis may be seen in mixed cases of stenosis and incompetence with a high pulmonary vascular resistance but is rare with pure incompetence

The *peripheral pulse* is small and often slightly water hammer in quality for there is a pronounced leak from the arterial system during systole Arteriograms in well developed cases show an abrupt upstroke measuring 0 05 to 0 07 second from the onset to the beginning of the blunt peak the peak itself is relatively brief occupying another 0 05 to 0 07 second the

down stroke proper is early beginning about 0 12 second after the onset of the pulse wave and tends to be precipitous (fig 10 01)

The *jugular venous pressure* is not infrequently raised in mitral incompetence when the pulmonary vascular resistance and heart rate are normal and when both pericardial effusion and tricuspid valve disease have been excluded In cases with normal rhythm *a* and *v* are about equal in amplitude and in those with atrial fibrillation the large *v* wave is followed by a steep *y* descent and conspicuous *y* trough In other words the form of the venous pulse is the same as that seen in congestive heart failure Under the circumstances mentioned a similar rise of venous pressure is rarely seen in cases of mitral stenosis Whether myocarditis or myocardial fibrosis is responsible, serious mitral incompetence signifying a more vicious primary rheumatic attack than simple stenosis or whether the phenomenon should be attributed to a filling defect of the right ventricle (Bernheim s syndrome) awaits solution In a typical example necropsy showed a huge dilated left ventricle a normal pulmonary artery a small right ventricle a normal tricuspid valve and a large distended right atrium the cavity of the right ventricle being greatly reduced by the bulged interventricular septum (fig 10 02) In the majority of mixed cases of mitral stenosis and incompetence a high venous pressure is associated with a high pulmonary vascular resistance around 6 to 9 units

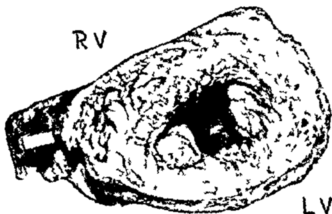
The *cardiac impulse* at the apex beat is hyperdynamic and displaced to the left and can hardly be confused with the impalpable left ventricle of mitral stenosis. If it is suspected that a very large right ventricle might be occupying the apex beat the question can be settled at once by consulting the electrocardiogram

On *auscultation* the characteristic signs of mitral incompetence are absence of a presystolic murmur a soft or normal first heart sound a loud apical pan systolic murmur embracing both first and second heart sounds and often accompanied by a palpable thrill absence of the opening snap of mitral stenosis a loud third heart sound and a short or absent mitral diastolic murmur

A *presystolic murmur* implies appreciable late ventricular filling and is *incompatible* with serious mitral incompetence

A loud *mitral first sound* with a normal P R interval or with atrial fibrillation implies a powerful potential or factual pressure gradient across the valve immediately before the left ventricle contracts a situation that is also incompatible with serious incompetence

The *systolic murmur* of mitral incompetence is usually loud and of fairly high frequency so that it is best heard with the Bowles type of stethoscope it is maximal at the apex beat over the surface of the left ventricle and outwards towards the axilla sometimes it is transmitted posteriorly over the surface of a greatly dilated left atrium The murmur necessarily begins with the mitral component of the first heart sound (fig 10 03) for the leak must commence as the valve tries to close This is some 0 05 second



(a) Transverse section showing great enlargement of the left ventricle and a small right ventricle



(b) Showing great distension of the right atrium

Fig 10 02—Photographs illustrating the Bernheim phenomenon in a fatal case of severe mitral incompetence

the aortic valve opens Again mitral incompetence must continue well into if not beyond the time of aortic valve closure for there is still a strong pressure gradient across the mitral valve at that moment, only as the rapidly falling left ventricular pressure approaches that in the left atrium should the leak stop (Brigden and Leatham 1953) Aortic systolic murmurs heard over the left ventricular apex beat start and finish earlier as described elsewhere (Leatham 1951) Tricuspid systolic murmurs heard over the right ventricular apex beat are also pan systolic but are accentuated during inspiration The pan systolic murmur of ventricular septal defect may be clinically identical with the mitral murmur in quality and timing but ordinarily occurs at the Roger area, well away from the apex beat when the heart is rotated clockwise in cases of ventricular septal defect however or anticlockwise in cases of mitral incompetence confusion is inevitable

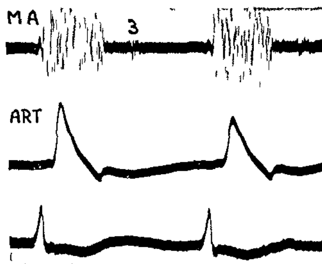


Fig 10 03—Phonocardogram in a case of mitral incompetence showing a pan systolic murmur and accentuated third heart sound (top tracing) The murmur starts with the mitral first sound well ahead of the arterial pulse (middle tracing) the electrocardiogram is seen below

The *absence of the opening snap* in serious mitral incompetence is generally attributed to the rigidity of the whole valve mechanism for there is certainly a sufficiently high pressure built up in the left atrium during ventricular systole to snap back the aortic cusp of the mitral valve as the pressure gradient between ventricle and atrium is abruptly reversed in early diastole This fibrous ankylosis also ensures a soft first heart sound even when the P R interval is short or after brief diastolic periods in cases with atrial fibrillation Heavy calcification so common in mixed cases enhances the effect (Wynn 1953)

A *third heart sound* usually loud was heard in 85 per cent of the author's series and is attributed to unusually rapid left ventricular filling Its occurrence in mitral incompetence was noted long ago by Sprague and White (1926)

Not enough attention is paid to the *duration of the mitral diastolic murmur* A murmur that completely fills diastole at a normal heart rate categorically denies serious mitral incompetence, for a long murmur means prolonged left ventricular filling Again a short atrio ventricular diastolic murmur is characteristic of unusually rapid ventricular filling whether the relevant atrioventricular valve is diseased or not as in thyrotoxicosis anæmia patent ductus, ventricular septal defect and atrial septal defect In serious *mitral incompetence the short murmur is often loud because the diseased* valve increases the turbulence set up by the torrent of blood that pours through the mitral orifice as soon as it opens but the flow virtually ceases almost as abruptly as it starts long before the next ventricular contraction because the ventricle is rapidly distended and the filling pressure falls off steeply[1] Thus a short mitral diastolic murmur, far from invalidating a diagnosis of pure mitral incompetence, is characteristic of it In cases of heavily calcified mitral valve disease with atrial fibrillation the length of the diastolic murmur and the presence or absence of the third heart sound become the only two auscultatory signs of any diagnostic significance for the pan systolic murmur gives no quantitative information and the absent presystolic murmur soft first heart sound and absent opening snap merely confirm the two circumstances mentioned

The electrocardiogram

In well developed cases the electrocardiogram shows an unobtrusive P mitrale and left ventricular preponderance (fig 10 04) In mixed border line cases of stenosis and incompetence with a pulmonary vascular resistance of 6 to 9 units slight right ventricular preponderance may be seen

RADIOLOGICAL APPEARANCES

The chief characteristics of mitral incompetence are an enlarged hyperdynamic, rapidly filled left ventricle associated with considerable dilatation and conspicuous pulsation of the left atrium (fig 10 05) In the anterior view the left atrium may be seen expanding during ventricular systole both *to the left and right (fig 4 42) It has become fashionable to deride this* sign but I have never seen the left atrium behave in this way in mitral stenosis or in any other condition In the first oblique view systolic expansion of the left atrium is common in mitral stenosis particularly when there is atrial fibrillation but even then the movement is not so abrupt nor the excursion so great as it often is with free incompetence Aneurysmal dilatation of the left atrium is also in favour of incompetence—although it may occur occasionally with pure stenosis The larger the left

Fig 10 04—The electrocardiogram in a case of severe mitral incompetence showing considerable left ventricular preponderance



Fig 10 05—Radiological appearances in a case of severe mitral incompetence showing considerable dilatation of the left atrium and left ventricle and marked pulmonary venous congestion

atrium, the less does it pulsate because the amount of regurgitant blood represents a smaller percentage of the left atrial volume

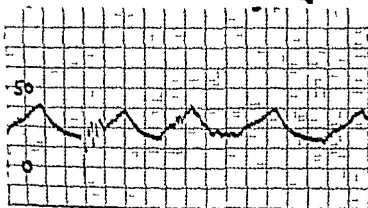
The aorta is usually rather small but less so than in mitral stenosis The pulmonary artery is rarely dilated except in cases of combined stenosis and incompetence with moderate elevation of the pulmonary vascular resistance The right atrium may be dilated if the venous pressure is raised as described previously Pulmonary venous congestion may be marked in severe cases especially when there is left ventricular failure but in the average case it is inconspicuous Heavy calcification of the mitral valve occurs in 50 per cent of cases with combined stenosis and incompetence but is uncommon with pure incompetence

Many attempts have been made to record the movements of the left atrium graphically either by means of electrokymography (e g Luisada and Fleischner 1948) or indirectly by means of an œsophageal pressure pulse tracing (e g Lassar and Loewe 1952 Zoob 1954) On the whole such methods have proved disappointing and have been discarded in most clinics perhaps prematurely

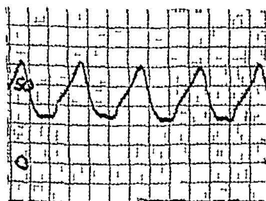
PHYSIOLOGICAL FINDINGS

Cardiac catheterisation usually reveals a raised left atrial pressure a normal or slightly raised pulmonary vascular resistance and a normal or low cardiac output The indirect left atrial pressure tracing obtained by the wedged catheter technique rewards careful study For several years these tracings did not seem to distinguish mitral stenosis from incompetence but attention had always been directed to the systolic part of the curve After studying the y descent of the venous and right atrial pressure pulses in a variety of conditions including tricuspid incompetence and tricuspid stenosis it was gradually established that the higher the filling pressure the steeper was the y descent and the more conspicuous the y trough *provided there was no obstruction at the tricuspid orifice* In tricuspid stenosis however the obstruction delayed ventricular filling and prevented rapid equalisation of atrial and ventricular pressures so that the y descent was relatively slow and the y trough inconspicuous indeed with severe stenosis there was no y trough at all the right atrial pressure continuing to fall after the *v* peak until interrupted by the next atrial or ventricular contraction a pressure gradient being demonstrable across the tricuspid valve throughout the whole of diastole It seemed virtually certain that obstruction of the mitral orifice would affect the left atrial pressure pulse in the same way i e in mitral stenosis the y descent should be slow and the y trough absent (fig 10 06) whereas in mitral incompetence or left ventricular failure the y descent should be rapid and the y trough conspicuous and early (fig 10 07) Careful analysis of technically satisfactory wedged pressure tracings and direct left atrial pressure tracings obtained at operation confirmed the thesis that obstruction to forward flow retarded

the rate of y descent and since the latter (Ry) was directly proportional to the height of v in all circumstances the degree of obstruction to forward flow was expressed as a ratio Ry v, Ry being measured in mm. Hg per second and v in mm Hg above the sternal angle In mitral stenosis the



Before valvotomy Ry v = 1 3



After valvotomy Ry v 3 3

Fig 10 06 —Left atrial pressure pulse before and after mitral valvotomy showing a change in the Ry v ratio from 1 3 to 3 3 after relief of the obstruction

ratio was commonly between 0 6 and 1 0 the extreme upper limit compatible with obstruction to forward flow being 1 6 (Owen and Wood 1955) In pure mitral incompetence left ventricular failure and Pick s disease the ratio usually lay between 2 and 6 Difficult borderline cases had ratios close to 1 6 It should be clearly understood that the Ry/v ratio is an index

of obstruction to forward flow only and that a figure demonstrating the absence of such obstruction does not distinguish mitral incompetence from left ventricular failure It has already proved its value, however, in helping to distinguish between dominant stenosis and dominant incompetence when both are present

Selective angiocardiography through a needle inserted directly into the left atrium through the posterior chest wall in the eighth intercostal space close to the vertebral column may show mitral incompetence clearly and gives a good idea of the actual size of the mitral aperture in systole and diastole (Bjork *et al* 1955)

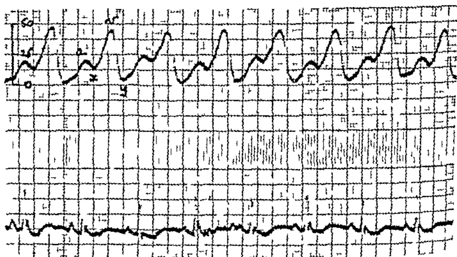


Fig 10 07—Left atrial pressure pulse in a case of mitral incompetence showing a very rapid y descent and conspicuous y trough the Ry y ratio is "

COMPLICATIONS

Pulmonary œdema hæmoptysis, angina pectoris and systemic embolism have already been discussed under *symptoms*

Atrial fibrillation is found in about a third of any average series of cases and is closely related to the age of the patient The great majority of patients over 50 years of age fibrillate Cases of mixed stenosis and incompetence fibrillate more than twice as frequently as cases of pure incompetence and more than one and a half times as frequently as cases of pure stenosis This may be a consequence of the greater severity of the original rheumatic onslaught in the mixed group or because the left atrium tends to be larger in these cases

The ventricular rate may be difficult to control with digitalis in severe cases of mitral incompetence with atrial fibrillation possibly because of the hyperdynamic behaviour of the left ventricle It may be worth pointing out that this difficulty is common to all hyperkinetic circulatory states complicated by atrial fibrillation, whether the left right or both ventricles

are involved, thus it may be encountered in patent ductus atrial septal defect and thyrotoxicosis to give an example from each group

Bacterial endocarditis seems to have a predilection for cases of mild mitral incompetence and may offer tragic proof of the organic nature of an apical systolic murmur hitherto regarded as functional Though the infection may be cured by means of penicillin or other antibiotics much damage has usually been inflicted by the time it is brought under control and serious mitral incompetence usually results

TREATMENT

No operative treatment yet devised has been of the slightest benefit to cases of mitral incompetence although heroic efforts have been made to repair the leak (e g Logan and Turner 1952) Nevertheless mitral incompetence is a simple mechanical fault and must remain a constant challenge to surgeons until it can be properly dealt with

Medical treatment and management are essentially the same as for mitral stenosis (q v)

MITRAL STENOSIS

INCIDENCE

Mitral stenosis with or without an unimportant leak is four times as common as virtually pure mitral incompetence and twice as common as combined stenosis and incompetence it accounts for 64 per cent of all cases of chronic mitral valve disease and for about 54 per cent of all cases of chronic rheumatic heart disease There are at least 100 000 cases of mitral stenosis in Great Britain between the ages of 18 and 44 and four fifths of them will require surgical treatment sooner or later (Wood 1954)

AGE AND SEX

Cowan and Ritchie (1935) who analysed 2 155 cases found that the frequency of chronic mitral valve disease in each decade up to the fifth was 2 19 21 19 and 16 per cent respectively, a further 23 per cent of cases occurring over the age of 50 The figures seem to be much the same for both stenosis and incompetence and in my own series the average age of all cases in each group was 37

The M F sex ratio for cases with pure mitral stenosis is 4 1 when there is trivial incompetence as well it falls to 3 1 and when there is serious incompetence to 1 1 In pure mitral incompetence males predominate the M F sex ratio then being 3 2 (Wood 1954)

LIFE HISTORY

A previous history of rheumatic fever subacute rheumatism or chorea is obtained in about 60 per cent of cases On the whole the more florid recurrent the original rheumatic state the worse the permanent valve

damage and the more probable serious mitral incompetence. Mild cases of pure mitral stenosis for example are twice as likely to have had isolated chorea as recurrent rheumatic fever whereas cases of combined stenosis and incompetence most of which have grossly disorganised valves are ten times more likely to have had recurrent rheumatic fever than isolated chorea

In my own series the average age of the initial rheumatic attack was 12 years the latent symptom free period 19 years the average age of onset of symptoms 31 years and the time spent in each of the first three grades of effort intolerance 2 7 2 7 and 1 94 years respectively total incapacity being reached 7 3 years after the onset of symptoms The average duration of total incapacity was about three years in 644 fatal cases of chronic rheumatic heart disease analysed by de Graff and Lingg (1935) and was *the same for mitral stenosis as for other valve lesions* There is of course considerable variation in individual cases but the general trend cannot be ignored

PATHOLOGY

Brock (1952) has referred to the monotonous regularity with which most cases of mitral stenosis submitted to operation have a small oval orifice measuring 1 × 0 5 cm In the simplest cases of pure stenosis the chief points of fusion are where the shortest stoutest and most direct chordæ tendineæ arising from the very summit of the papillary muscles join the margins of the cusps on each side of what Brock has called the central pathway of the mitral valve These two critical areas of tendon insertion are about 2 cm apart which means that the central pathway through which most of the blood normally enters the left ventricle is only about 3 sq cm in cross section and lateral to this there is relatively little flow the commissures acting merely as hinges allowing the central parts of the cusps to open widely In a mild attack of rheumatic carditis the only damage to the valve may be along the line of closure of the cusps just proximal to their free margins where they receive the maximum natural trauma Perhaps as the result of deposition of platelets and fibrin on the surface of this damaged zone a stickiness develops which encourages the two cusps to adhere to one another where they meet most firmly The strong blood flow through the central pathway prevents fusion at the centre but there is less resistance to fusion at the critical areas of tendon insertion on each side of the central pathway and there is good reason to believe that this is where the two cusps first stick together The lateral parts of the valve are usually spared in a mild attack of rheumatic fever and have no reason to adhere of themselves nor has lateral fusion alone ever been observed Once the two cusps are held together at the critical areas of tendon insertion however their lateral parts necessarily come into permanent apposition and since there is little or no flow in this zone to prevent it light lateral adhesions then form The result is fusion of the

two cusps from the ring to the edges of the central pathway Since the hinge like action of the lateral parts of the valve can no longer function the central portion of the two cusps cannot open fully the aperture thus becomes oval and cannot measure much more than 2×1 cm in the mildest cases Gradual reduction in the size of the lumen between the two critical areas of tendon insertion may result from repeated deposits of fibrin at the edges the excrescences becoming covered by endothelium and then fibrosed as described by Magarey (1951)

This attractive hypothesis so ably presented by Brock (1952) leaves one important question and its corollaries unanswered When does cross fusion of the critical areas of tendon insertion occur? If it is during the stage of active carditis which the hypothesis favours why does the initial 2×1 cm stenosis give rise to no physical signs? There is ample proof that a presystolic murmur and loud first heart sound occur when stenosis is trivial the cardiac output normal and the left atrial pressure around 5 mm Hg with reference to the sternal angle If on the other hand the stenosis develops when it seems to i e some 5 to 10 years after the initial attack why should sudden fusion of the critical areas of tendon insertion occur then at a time when the surface of the cusps should have no cause for stickiness? If the hypothesis is correct it would seem that initial fusion of the critical zones would have to occur during the active stage but that this would not result in physiological stenosis This is quite likely especially if the initial points of fusion were 2 5 cm apart for the central pathway of the mitral valve would then be as large as the aortic orifice assuming that the central parts of the cusps were able to open widely enough Physiological stenosis with a pressure gradient across the valve would then develop slowly and variably over the years according to the speed with which the commissures of the oval orifice gradually silted up From experience gained at operation mild physiological stenosis, with typical physical signs but no symptoms occurs when the oval orifice is between 1 5 and 2 cm in length and perhaps half this in width Critical stenosis requiring valvotomy is associated with an oval orifice averaging 1× 0 5 cm , as repeatedly pointed out by Brock By extreme stenosis is meant an orifice materially smaller than this in the region of 5×3 mm Although Brock has criticised the terms mild average and severe stenosis when used with the intention of conveying some idea of the degree of stricture present rather than the patient s disability in the author s view their use with just this meaning is thoroughly justified A simple mathematical sum will show that a relatively mild stenosis measuring 1 5×0 75 cm is more than twice as large as an average orifice of 1×0 5 cm and nearly eight times as large as a severe stricture measuring 5×3 mm

Whether gradually increasing stenosis results chiefly from the effects of continued smouldering activity or whether it is a more or less inevitable secondary change due to repeated deposition of fibrin on a damaged area has yet to be settled

HÆMODYNAMICS

Initial cross fusion of the critical areas of tendon insertion during the stage of active carditis leaves a sufficiently large central pathway probably measuring 2 5×1 5 cm through which a normal blood flow can be maintained without any form of compensation According to the Gorlin formula such an orifice which would measure about 2 5 sq cm in cross section would allow a blood flow of 6 8 litres per minute with a left ventricular filling pressure of 6 mm Hg and a heart rate of 70 to 80 beats per minute *As the commissures of this oval orifice gradually silt up the size of the* aperture dwindles until it begins to obstruct the blood flow The left atrial *pressure then rises a few mm Hg and wholly compensates for the obstruc*tion It is calculated that an oval orifice measuring 2–2 25×1 cm is small enough to cause this grade 1 physiological stenosis Physical signs (presystolic murmur and accentuated first heart sound) first develop at this stage which is ordinarily some 3 to 10 years after the original rheumatic attack Grade 2 or moderate stenosis implies an oval aperture measuring 1 5–1 75×0 75–0 9 cm This too is easily compensated for by a further rise of left atrial pressure which at rest is found to be around 10 mm Hg above the sternal angle Under ordinary circumstances there are no symptoms but the auscultatory physical signs of mitral stenosis are now complete, the opening snap being easily heard and the mitral diastolic murmur occupying practically the whole of diastole The elevated left atrial pressure is associated with a similar rise of pulmonary venous pressure pulmonary capillary pressure and pulmonary arterial pressure the pulmonary arterio venous pressure gradient remaining normal (about *10 mm Hg*)

On strenuous exercise there is some danger of unexpected acute pul*monary œdema in these cases of moderate severity for no protective* mechanisms have yet come into play It may be calculated for example that a cardiac output of 16 litres per minute with a heart rate of 120 would raise the left atrial pressure to 35 mm Hg above the sternal angle if the mitral aperture was 1 5 cm With no acquired barrier between pulmonary capillaries and alveoli a capillary pressure of this level which is above the osmotic pressure of the plasma must cause pulmonary œdema Practical experience supports these statements

Grade 3 or considerable stenosis is the classic text book type According to Brock and other surgeons the valve in these typical dyspnœic cases measures about 1×0 5 cm but physiological calculations suggest it is *more likely to have a cross section of* 0 75 sq cm *which means dimensions* nearer 1 5×0 75 cm Dexter s group puts the critical orifice at 1 cm² *which implies an oval aperture measuring about 1 75×0 85 cm* (Lewis *et al* 1952) [The discrepancy between physiological calculations and surgeons estimates is consistent with all grades of stenosis Post mortem measurements are closer to physiological expectations] Under these circumstances an adequate cardiac output can only be maintained with a

left atrial pressure around 20 to 25 mm Hg above the sternal angle at rest. This causes pulmonary venous congestion and its consequences. Exercise, excitement, pregnancy, or simple tachycardia (which diminishes the ventricular diastolic filling time) results in considerable further elevation of the pulmonary venous pressure, which may rise well above the osmotic pressure of the plasma (30 mm Hg). At this stage a proportion of patients die from acute pulmonary œdema, but the majority do not because certain mechanisms come into play which serve to protect the lungs and it is important to understand just what these are.

If the mean left atrial pressure is 30 mm Hg, the mean pressure in the pulmonary artery must be at least 40 mm Hg if the necessary gradient between the two is to be preserved. In acute experiments this passive pulmonary hypertension, as it may be called, maintains a linear relationship to the left atrial pressure at all levels (Lasser and Loewe, 1954) and this is the rule in chronic cases (Wood, 1954). In 28 per cent of individual, however, as soon as the left atrial pressure begins to rise at all seriously the pulmonary arterioles constrict. This obstructs the circulation proximal to the pulmonary capillaries and so prevents their developing dangerously high pressures. In response to the high pulmonary vascular resistance the pulmonary blood pressure rises considerably and may reach systemic level. This puts a heavy burden on the right ventricle, which sooner or later fails. Thus by this mechanism early death from acute pulmonary œdema is prevented at the cost of a low cardiac output and ultimate right ventricular failure.

A second change that tends to prevent pulmonary œdema is the development of a physical barrier between the capillaries and alveoli, the capillary wall, interstitial tissue and alveolar basement membrane all becoming thickened, so that it becomes increasingly difficult for fluid to enter the alveoli even though it may pass into the interstitial tissue (Hayward, 1955). This helps to explain why acute pulmonary œdema is usually an early symptom, and why attacks tend to cease spontaneously if life can be preserved long enough for this barrier to be erected. Fluid is removed from the interstitial tissue by the lymphatics, which themselves become engorged.

The very high left atrial pressures that may develop on exercise in these stereotyped cases of mitral stenosis, even as high as 60 mm Hg, seem to deny the importance of a broncho pulmonary venous shunt mechanism which theoretically might relieve pulmonary venous congestion. According to Marchand, Gilroy and Wilson (1950) the true bronchial veins within *the substance of the lung drain directly into the pulmonary veins*, so that the bronchial venous pressure must be the same as the pulmonary venous pressure. This may explain early hæmoptysis in mitral stenosis, but provides no basis for belief in a shunt mechanism that might relieve the pulmonary venous pressure. However, these workers also confirmed that the extrapulmonary bronchial veins, which they called the pleuro hilar veins, drained into the azygos, hemiazygos and intercostal veins and

communicated freely with the pulmonary veins as previously described by Miller (1947) and others in mitral stenosis the pleuro-hilar bronchial veins were dilated and sometimes tortuous and varicose (Gilroy Marchand and Wilson 1952) It must be admitted then that the pulmonary venous circulation is in fact provided with a safety valve at the root of the lung and that when well developed this could lower the pulmonary venous pressure at the expense of the cardiac output Patients relieved of pulmonary congestion in this way should complain of fatigue and perhaps œdema when the pulmonary venous pressure is only moderately raised the pulmonary vascular resistance normal and the estimated cardiac output normal when based on an A V difference calculated from samples obtained from the pulmonary artery right ventricle or right atrium From such physiological data the physician would conclude that stenosis was mild and that the symptoms must have some other explanation Only unexplained enlargement of the right ventricle might point to the true state of affairs unless samples obtained from the superior vena cava above and below the junction of the azygos vein proved the existence of a significant broncho pulmonary shunt as when an anomalous pulmonary vein joins the azygos No physiological studies on this point have yet been reported but two observations may be mentioned (1) I have not myself been able to detect much difference between high and low superior vena cava samples in several cases of mitral stenosis in which the possibility of a broncho pulmonary shunt was considered (2) in the few cases of mitral stenosis in which unexplained enlargement of the right ventricle has been associated with a relatively low pulmonary venous pressure and a normal pulmonary vascular resistance the cardiac output based on routine pulmonary artery samples has been low and has failed to rise properly on exercise so that a myocardial fault has been invoked (Harvey *et al* 1955) This myocardial dysfunction may be due to active carditis or residual fibrosis, and may be regarded as the fourth factor that tends to protect the lungs

To sum up it must be repeated that in the typical case of critical mitral stenosis the usual problem is not why the pulmonary venous pressure is lower than expected but why pulmonary œdema does not develop when the pulmonary venous pressure rises well above the osmotic pressure of the plasma and the answer to this may lie in the development of a physical barrier between the capillaries and alveoli A high pulmonary vascular resistance explains the behaviour of the vast majority of cases in which elevation of the left atrial pressure is limited the right ventricle large and the cardiac output low and a myocardial fault adequately explains the remainder There may or may not be a small group of cases that are materially influenced by the development of a broncho pulmonary venous shunt This might be best detected by analysing low S V C samples for traces of Evans blue dye a few seconds after injecting a suitable quantity into the pulmonary artery

SYMPTOMS

The chief symptom of mitral stenosis is *dyspnœa* This appears to be due to increased rigidity of the lungs so that the intrathoracic pressure swings have to be greater than normal in order to inflate and deflate the lungs (Marshall McIlroy and Christie 1954) in other words respiration becomes laborious and ventilation on effort readily approaches 50 per cent of the maximum breathing capacity The increased rigidity is apparently caused by changes in the interstitial tissue including chronic interstitial œdema (Hayward 1955) for the pulmonary blood volume is normal (Lagerlof *et al* 1949) The extra space occupied by the interstitial tissue reduces the vital capacity and total lung volume Œdema of the bronchial mucosa with or without broncho spasm due to the high intrapulmonary bronchial venous pressure (Marchand *et al* 1950) adds to the ventilatory difficulty Except during attacks of acute pulmonary œdema the arterial pO pCO and pH are usually normal Whether stretch receptors are stimulated by the changes in the interstitial tissue and excite the Hering Breuer reflex inhibiting the depth of inspiration is uncertain

The degree of dyspnœa on effort usually determines the clinical grading of effort intolerance in mitral stenosis Four grades are commonly recognised corresponding to the four adjectives of degree—slight moderate considerable and gross In grade I symptoms are provoked by more than average activity e g running hurrying walking up hills playing games polishing or scrubbing Patients in this grade usually undertake the activities that make them breathless but cannot compete with their fellows In grade II symptoms occur on ordinary activity such as walking at an average pace or up two flights of stairs carrying a shopping basket dancing and any form of manual labour Patients in this grade limit their physical activities but can still lead an almost normal social life In grade III symptoms develop with less than ordinary physical activity and force patients to walk slowly on the level shopping and all but the lightest housework is abandoned Grade IV means total incapacity

Orthopnœa occurs in 70 per cent of cases in grades III or IV Sitting up especially with the legs down lowers the right atrial pressure and thus diminishes the output of the right ventricle This in turn lowers the left atrial pressure and therefore the pulmonary venous and capillary pressures In the horizontal position these effects are reversed so that transudation of fluid from the pulmonary capillaries into the interstitial tissue is encouraged Although Donald *et al* (1953) have denied that sitting up in bed lowers the cardiac output sufficiently to be of any importance they noted that in cases of mitral stenosis it resulted in a marked fall of pulmonary artery pressure which certainly suggests a drop in output

Attacks of frank pulmonary œdema occur in about 10 per cent of all cases of mitral stenosis in which the mitral orifice is more or less critically reduced (Wood 1954) Precipitating agents include effort emotion sexual intercourse pregnancy respiratory infections uncontrolled atrial fibrilla

tion and anæsthesia Physiologically the most important provocative factors are tachycardia, which reduces the left ventricular diastolic filling time hydræmia a rise of cardiac output and perhaps some neurogenic or chemical disturbance which alters capillary permeability Physiological data during an attack are necessarily limited but the left atrial pressure is usually between 30 and 50 mm Hg and always well above the osmotic pressure of the plasma the heart rate is nearly always 120 or more beats per minute the cardiac output is higher than usual and the pulmonary vascular resistance commonly normal The transudate is believed to be much the same kind of fluid that normally passes through the capillary walls into the tissue spaces which in the interstitial tissues of mammalian lung contains 2 5 to 3 G per cent of protein (Warren and Drinker, 1942 Drinker 1945) As the attack proceeds the arterial oxygen saturation gradually falls and in severe cases may become as low as 50 per cent at the beginning of the attack, however it is normal so that anoxia cannot be blamed for initiating events by increasing the permeability of the capillary walls By having this effect later in the attack, however anoxia could well establish a vicious circle were it not for the fact that it also causes a sharp rise of pulmonary vascular resistance (Liljestrand 1948) which must tend to lower the capillary pressure and terminate the attack Limited evidence that the pulmonary vascular resistance does not rise during spontaneous attacks of pulmonary œdema should be accepted with considerable reserve because these cases are very difficult to investigate

Protective mechanisms or complications tending to prevent acute pulmonary œdema include a high pulmonary vascular resistance the development of a capillary alveolar interstitial barrier atrial fibrillation when controlled by means of digitalis, myocarditis or cardiac fibrosis, associated tricuspid stenosis and perhaps a broncho pulmonary venous shunt

The most important of these is probably a high pulmonary vascular resistance In my own series this averaged 2 9 units in cases giving a history of pulmonary œdema and never exceeded 5 2 units whereas in patients who had never had orthopnœa paroxysmal dyspnœa or frank pulmonary œdema but whose stenosis was no less severe it averaged 9 2 units

Clinically acute pulmonary œdema occurs characteristically in young women with an average grade of stenosis relatively early in its course before protective mechanisms have had time to develop Thus the average age of patients with pulmonary œdema in the author s series was 32 compared with 37 for the series as a whole Normal rhythm is nearly twice as frequent as atrial fibrillation despite the fact that the onset of the latter may precipitate acute pulmonary œdema The attack itself may start insidiously with slight dyspnœa orthopnœa and a gentle repetitive cough (stage A) but soon develops strongly dyspnœa becoming extreme and often accompanied by wheezing (cardiac asthma) the face pales the heart rate quickens the blood pressure rises, the extremities turn cold and blue and the heart

pounds (stage 2) The patient becomes greatly distressed and frightened and as suffocation increases fine crepitations become widespread and quantities of frothy white or pink fluid may be expectorated (stage 3) Central cyanosis appears late in the attack, and if the arterial oxygen saturation falls sufficiently the vasomotor centre may fail, and a state of collapse sets in the blood pressure falls the skin becomes grey cold and wet the pulse almost imperceptible and the respirations shallow (stage 4) If treatment fails the patient finally sinks into a state of unconsciousness and dies

Paroxysmal cardiac dyspnœa is similar, but transudation of fluid from the capillaries does not enter the alveoli being prevented from doing so by the physical barrier described earlier Interstitial œdema makes the lungs very rigid and breathing is laboured but there are no crepitations no fluid is expectorated and the arterial oxygen saturation falls little if at all

Thus orthopnœa paroxysmal cardiac dyspnœa and acute pulmonary œdema are all manifestations of a tendency for fluid to pass out of the pulmonary capillaries into the interstitial tissue of the lung Although from the patient s point of view the order in which they have just been given represents an increasing grade of severity, the disease as a whole is usually most advanced when there is orthopnœa only, and least advanced when there are attacks of acute pulmonary œdema cases of paroxysmal cardiac dyspnœa occupying a middle position The reason for this has already been explained

Hæmoptysis

There are five kinds of hæmoptysis complicating mitral valve disease (1) the sudden unexpected profuse hæmorrhage known as pulmonary apoplexy (2) blood streaked mucoid sputum associated with winter bronchitis (3) blood stained sputum associated with attacks of paroxysmal cardiac dyspnœa (4) pink frothy sputum accompanying acute pulmonary œdema (5) frank hæmoptysis due to pulmonary infarction

A history of *pulmonary apoplexy* is obtained in one quarter of cases severe enough to warrant valvotomy It is characteristically an early symptom often the very first and although usually recurrent attacks tend to cease spontaneously after two or three years The most important precipitating agents are pregnancy and physical effort but at least half of the attacks occur without warning and for no reason known to the patient

The hæmorrhage itself is sudden and profuse the amount of blood coughed up being usually measured in ounces It is rarely dangerous and tends to stop spontaneously within half an hour or so although residual blood may stain the sputum for a day or two

Pulmonary apoplexy is attributed to rupture of a small intrapulmonary bronchial vein as a result of a rather sudden rise of left atrial pressure for which the pulmonary and bronchial venous systems are unprepared In the early stage of mitral stenosis as in normal individuals these vessels

are very thin walled after being subjected to an increased pressure for several years however their walls thicken appreciably (Henry 1952) and this may be one reason why attacks occur relatively early and after two or three years tend to cease spontaneously Rupture of a dilated pleuro hilar vein which is in anastomotic communication with the pulmonary venous system is another and perhaps more likely source of profuse hæmorrhage for these small veins are forced to carry more than their fair share of blood and though not subjected to high pressure are often varicose (Gilroy *et al* 1952) The fall in pulmonary venous pressure likely to result from a brisk hæmorrhage may well discourage further bleeding

As pointed out by Thompson and Stewart (1951) hæmoptysis of this kind is not a sign of pulmonary hypertension On the contrary it is exceedingly rare when the pulmonary vascular resistance is over 10 units for the pulmonary venous system is then protected (Wood 1954)

Congestive hæmoptysis is a convenient title for blood stained sputum accompanying an attack of acute bronchitis paroxysmal dyspnœa or pulmonary œdema The mild hæmorrhage in these cases is never as important as the condition with which it is associated The ruptured vessels are presumably very small for hæmorrhage is never profuse with bronchitis and paroxysmal dyspnœa a bronchial vessel is almost certainly at fault with acute pulmonary œdema however the uniformly pink froth suggests capillary rupture into alveoli

Hæmoptysis due to pulmonary infarction is a late complication of mitral stenosis and is usually caused by an embolus secondary to phlebo thrombosis in the legs in advanced cases with heart failure This will be discussed later

Winter bronchitis

Recurrent attacks of winter bronchitis occur in about a third of cases of well developed mitral stenosis Cough with blood stained sputum wheez ing and breathlessness may be very distressing The turgid or œdematous state of the bronchial mucosa caused by the high bronchial venous pressure is believed to be responsible for the severity of symptoms if not for the susceptibility to infection although a convincing relationship between the frequency of bronchitis and the height of the left atrial pressure cannot be demonstrated statistically (Wood 1954) Compression of the left bronchus by a greatly dilated left atrium which has been known to cause collapse of the left lung (King 1838) or splaying of either bronchus plays little part in the syndrome

It is unusual for recurrent bronchitis to have any permanent ill effect on lung function or the pulmonary circulation in cases of mitral stenosis and fears that bronchitis may be primary or that secondary bronchitis has already caused emphysema and cor pulmonale are rarely justified On the contrary one of the many remarkable results of technically successful valvotomy is the abolition of these tiresome attacks

Systemic embolism

In any large series of living cases of mitral stenosis a history of systemic embolism is likely to be obtained in 9 to 14 per cent (Sellors Bedford and Somerville 1953 Wood 1954) The embolism is cerebral in at least 60 per cent of instances visceral in 10 per cent and peripheral in 30 per cent In about 20 per cent of afflicted cases emboli are multiple and in 60 per cent recurrent (Daley *et al* 1951 Wood 1954)

Atrial fibrillation is a contributing factor in about three quarters of all cases and *is particularly dangerous at its onset when the ventricular rate* is uncontrolled

Little correlation has been found between the size of the left atrium or of its appendage and the frequency of embolism and giant left atria are rarely to blame There is no correlation between the incidence of embolism and the pulmonary vascular resistance or the size of the mitral orifice Embolism may be the first symptom of mitral stenosis occurring at a time when there is no effort intolerance and when the rest of the data indicate a relatively mild stricture this was so in 12 5 per cent of embolic cases studied by the author

At operation a clot in the left atrium or its appendage is found in about 2 per cent of all cases whether there has been a history of embolism or not Left atrial thrombi are admittedly nearly twice as common in post mortem material (Wallach *et al* 1953) but even then some 36 per cent of cases with a history of embolism have none (Daley *et al* 1951) Operative embolism the frequency of which has dwindled from 10 to 5 per cent as more effective precautionary measures have been taken is no more common in patients with a history of embolism than in those without

All this suggests that only fresh clots are likely to be flung out into the systemic circulation and that once a thrombus is organised there is no further spontaneous danger from that source only the surgeon s finger is liable to dislodge a fragment of old thrombus

The local effects of systemic embolism have been described briefly in chapter I It may be added here that out of 20 cases of cerebral embolism occurring in patients already under observation in mitral valve disease only two died and that the 49 per cent mortality cited by Daley *et al* (1951) may well be biased by selected and post mortem material When trying to prevent cerebral embolism during valvotomy both carotids should be temporarily occluded at critical moments because experimental and necropsy evidence proves that emboli may pass into either carotid impartially (Hall Dencker and Biorck 1952)

Angina pectoris

Cardiac pain indistinguishable in all respects from that encountered in occlusive-coronary disease occurs in about 10 per cent of cases of mitral stenosis that are otherwise severe enough to warrant valvotomy it does not occur in mild cases The angina is not caused by coincidental coron

atherosclerosis because the sex ratio of affected cases is 5 1 in favour of women, their average age is 36 pain always disappears following technically successful valvotomy and in a limited number that have come to necropsy the coronary arteries have been normal Angina is twice as common in cases with a high pulmonary vascular resistance as in those without and also twice as common in cases with extreme stenosis as in those with an average stricture It is tentatively attributed to functional impairment of the coronary blood flow due to strict limitation of the cardiac output and is believed to affect the left ventricle more than the right as long as the pulmonary artery pressure on effort is lower than the aortic (Wood 1954)

Left vocal cord paralysis (Ortner's syndrome)

Huskiness of the voice due to paralysis of the left recurrent laryngeal nerve occurs in about 0 5 per cent of cases of mitral stenosis Ortner (1897) thought that the nerve was compressed by the dilated left atrium and essentially this may be true but the actual compression is usually mediated by enlarged tracheo-bronchial lymph nodes (Dolowitz and Lewis 1948) and dilatation of the pulmonary artery is often contributory (Fetterolf and Norris 1911) The voice may improve post operatively (Ari Harvey and Hufnagel 1955)

Atrial fibrillation

Rapid irregular palpitations in cases of mitral stenosis are commonly due to paroxysmal or uncontrolled atrial fibrillation The abnormality of rhythm occurs in about 40 per cent of all cases and is related chiefly to the age of the patient, not to the degree of stricture (de la Chapelle Graefe and Rottino 1934) My own findings in live cases agreed almost exactly with those of the authors cited in addition left atrial biopsies denied that rheumatic activity played any part in encouraging atrial fibrillation even in the youngest adults and more than average left and right atrial dilatation could be interpreted as a result rather more easily than as a cause of the rhythm change

Uncontrolled atrial fibrillation may cause acute dyspnœa because the rapid heart rate tends to increase the output of the right ventricle while depriving the left of sufficient diastolic time in which to fill it should be understood that shortening diastole interferes little with ventricular filling when the atrioventricular valve is normal but considerably when it is stenosed

When the pulmonary vascular resistance is high atrial fibrillation with a rapid ventricular rate usually causes congestive heart failure the tendency for the left atrial pressure to rise secondary to the increased rate is offset by the diminished right ventricular output so that fatigue œdema and swelling of the abdomen overshadow breathlessness The cardiac output may be very low in these cases because the shortened left ventricular diastolic filling time is not compensated for by an adequate rise of left atrial pressure

When the ventricular rate is controlled by means of digitalis these physiological difficulties are removed and recovery is prompt This is why digitalis has always been expecially renowned for the benefit it bestows on cases of *rheumatic heart disease* with atrial fibrillation

The circulatory hold up when the ventricular rate is very fast also explains the frequency of fresh thrombosis in the left atrium at this time and the immediate danger of embolism

PHYSICAL SIGNS

Mitral facies and cold blue hands

Peripheral cyanosis in the face and hands is due to peripheral vaso constriction secondary to a low cardiac output and is therefore seen especially in cases with a high pulmonary vascular resistance it is not a feature of uncomplicated mitral stenosis of average severity in which a fair output is maintained with the help of a high left atrial pressure In advanced pulmonary hypertensive cases the hands may be warm and the palms bright red as a result of impaired hepatic function

Loss of weight is usual in severe mitral stenosis unless counterbalanced by œdema and the lean features contribute to the mitral facies

Peripheral pulse

The brachial pulse in all well developed cases of mitral stenosis is small in volume but well sustained in quality except in advanced cases with pulmonary hypertension and chronic heart failure when vasodilatation due to impaired hepatic function may modify it

Jugular venous pressure and pulse

In simple mitral stenosis the systemic venous pressure and the jugular pulse are both normal The venous pressure may rise however as a result of improperly controlled atrial fibrillation severe pulmonary hypertension or associated tricuspid stenosis Heart failure due to myocarditis or cardiac fibrosis is rare

With uncontrolled atrial fibrillation the x descent of the jugular pulse disappears v begins earlier and is followed by y so that there is only one crest and one trough per cardiac cycle the higher the v wave the quicker the y descent and the more conspicuous the y trough

Both pulmonary hypertension and tricuspid stenosis usually give rise to a giant *a* wave when there is normal rhythm with atrial fibrillation however cases of pulmonary hypertension show a rapid y descent and deep y trough whereas cases of tricuspid stenosis show a relatively slow y descent and absent y trough

Cardiac impulse

The left ventricle is characteristically impalpable in cases of pure mitral stenosis only the tap of the first heart sound being appreciated in the

region of the mid clavicular or anterior axillary line The degree of right ventricular thrust in the left parasternal line is proportional to the pulmonary vascular resistance passive pulmonary hypertension causes very little right ventricular enlargement and a dilated left atrium posteriorly only pushes the heart forwards appreciably when it is aneurysmal Pulsation over the pulmonary artery is rare and when present means an extreme pulmonary vascular resistance

Auscultation

There are four important auscultatory signs of mitral stenosis—a presystolic murmur a loud first heart sound an opening snap and a mitral diastolic murmur (fig 10 08)

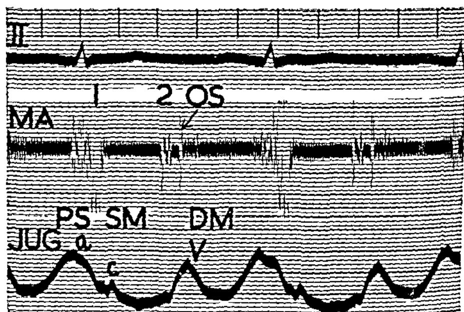


Fig 10 08– Phonocardiogram from a case of mitral stenosis showing a crescendo presystolic murmur loud first sound opening snap and mid diastolic murmur timed against the electrocardiogram and phlebogram

(By courtesy of Dr Aubrey Leatham)

A *mitral presystolic* (Fauvel 1843) *or left atrio systolic* (Gairdner 1861) *murmur* can be heard in practically all cases of physiological mitral stenosis with normal rhythm even when the stricture is so mild as to be associated with a left atrial pressure of only 5 mm Hg above the sternal angle It is occasionally masked by gross enlargement of the right ventricle secondary to an extreme pulmonary vascular resistance for the left ventricle may then be displaced so far posteriorly that mitral events cannot be heard at the apex beat which is usurped by the right ventricle

The *first heart sound is accentuated* in practically all cases of more or less

pure mitral stenosis provided the valve is not heavily calcified In conjunction with the presystolic murmur a loud first sound can be heard in the mildest cases with left atrial pressures only a few mm Hg above the sternal angle The late diastolic or presystolic atrio ventricular pressure gradient forces the mitral cusps to remain wide open to the very end of diastole so that when the left ventricle contracts they slam together Heavily calcified valves are usually so rigid that very little movement of the cusps is possible

In cases with atrial fibrillation the presystolic atrio ventricular pressure gradient and therefore the intensity of the first sound varies inversely with the length of the preceding diastole as pointed out by Ravin and Bershof (1951) Exceptionally however the intensity of the first heart sound does

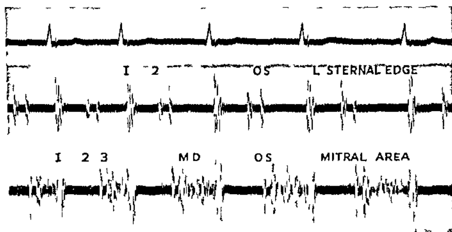


Fig 10 09—Phonocardiogram showing an opening snap followed by a mitral diastolic murmur in a case of mitral stenosis with atrial fibrillation

not vary or it may have a paradoxical relationship to the length of the preceding cycle Such behaviour has not been satisfactorily explained but it suggests relative fixation of the cusps so that they may not be able to billow into the ventricle beyond certain narrow limits whatever the atrio ventricular pressure gradient the intensity of the first sound then varies inversely with the pressure gradient for the cusps close more sharply when the left ventricle is full and the left atrial pressure relatively low than when the left ventricle is half empty and the left atrial pressure high

The first heart sound is also slightly delayed in mitral stenosis because the first 0 01 second or so of systole is occupied with raising the left ventricular pressure to atrial level (Cossio and Berconsky 1943) In cases with atrial fibrillation the delay varies inversely with the length of the preceding cycle (Messer *et al* 1951)

The *opening snap* of Potain is a sharp high pitched sound made by the aortic cusp of the mitral valve when it is flung forwards into the cavity of the left ventricle as the atrio ventricular pressure gradient is reversed at the end of the period of isometric relaxation and therefore coincides temporally with the summit of the *v* wave of the left atrial pressure pulse (Margolies and Wolferth 1932) It occurs 0 06 to 0 14 second (usually 0 08 to 0 10 second) after aortic valve closure (Braun Menendez and Orias 1935) and is best heard down the left sternal border over the root of the aorta or at the apex beat (fig 10 09) The interval between the aortic second sound and the opening snap is inversely proportional to the height of the left atrial pressure and therefore directly proportional to the length of the preceding cardiac cycle (Messer *et al* 1951) Thus if due allowance is made for cycle length (disregarding the cardiac output and the pulmonary vascular resistance), the more delayed the first heart sound and the earlier the opening snap the tighter is the mitral stenosis (Wells 1954)

The opening snap is heard in practically all cases of pure mitral stenosis of more than trivial degree, provided the valve is not heavily calcified and rigid Exceptionally an extreme pulmonary vascular resistance masks the snap because a greatly enlarged right ventricle tends to prevent transmission of mitral sounds to the anterior chest wall The opening snap may also be absent when there is associated aortic incompetence probably because the regurgitant jet interferes with the forward movement of the aortic cusp of the mitral valve

An *apical mid diastolic murmur* is heard in all well developed cases of mitral stenosis unless masked by a greatly enlarged right ventricle or a loud aortic diastolic murmur transmitted to the apex It is usually low pitched and is heard best with the bell stethoscope when the patient lies on the left side The murmur is not prevented by heavy calcification nor altered by atrial fibrillation It begins just after the opening snap its onset coinciding with the period of rapid ventricular filling i e with the steep part of the y descent (downstroke of v) It therefore gives rise to a form of triple rhythm the cadence of which is very characteristic whether preceded by an opening snap or not

Neither the intensity of the murmur nor the presence of a thrill matters much but the length of the murmur is very important In mild cases the murmur is relatively short ending as soon as left atrial and ventricular diastolic pressures equalise in more severe cases it extends right up to the next first heart sound for left atrial and ventricular diastolic pressures do not equalise at all The length of the murmur is easiest to gauge in cases with atrial fibrillation for there is then no interference from atrial systole and from time to time long pauses facilitate analysis

THE ELECTROCARDIOGRAM

A well defined P mitrale (fig 10 10) is seen in practically all cases of moderate or severe mitral stenosis with normal rhythm but is usually

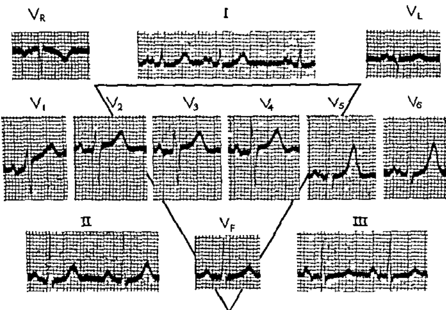


Fig 10 10—Electrocardiogram in a case of mitral stenosi showing \ idened bifid P waves particularly in leads 1 2 V₅ and V

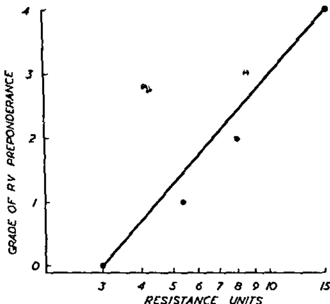


Fig 10 11—Graph show ng th relationship between the electrocardiographic grade of right ventricular prepondera ice and the pulmonary vascular resistance in cases of mitral stenos s (semi logarithmic scale)

absent in mild cases The P wave is bifid and widened to 0 12 second the first peak representing right atrial activation the second left atrial activation (Reynolds 1953) The voltage is usually normal

Tall peaked P waves in cases of mitral stenosis indicate a high pulmonary vascular resistance or associated tricuspid stenosis

The ventricular complexes are strictly normal in uncomplicated cases unless the S T segments are depressed by digitalis therapy Right ventricular preponderance means pulmonary hypertension secondary to a raised pulmonary vascular resistance the degree of each correlating very closely with one another (fig 10 11) Passive pulmonary hypertension does not cause right ventricular preponderance

RADIOLOGICAL APPEARANCES

X rays reveal characteristic changes in the size shape and behaviour of the heart and great vessels and in the appearances of the lungs, which taken together are seen in no other condition

The *aorta* is small unless the patient is over 45 years old or unless the stenosis is sufficiently mild to allow a normal resting cardiac output

The *left ventricle* is inconspicuous hypodynamic and fills relatively slowly Apparent enlargement in otherwise uncomplicated cases of pure stenosis is usually an erroneous interpretation of a shadow that may represent pericardial effusion or a greatly enlarged right ventricle that is occupying the apex beat occasionally it is genuine and may then be due to previous mitral incompetence or unusually severe carditis

The left atrium is dilated in all but the mildest cases In the anterior view it may be seen on both borders of the heart forming a hump between the pulmonary arc and left ventricle on the left side and lying above and overlapping the right atrium on the right side (fig 10 12) In the lateral or oblique positions a dilated left atrium displaces the barium filled œsophagus backwards (fig 10 13) Rarely the whole chamber is sharply outlined as a result of endocardial calcification

The degree of left atrial enlargement is not related to the severity of the stenosis The left atrium is apt to be relatively small in cases of pure stenosis in young adults with normal rhythm and a tendency to develop pulmonary œdema and in cases with an extreme pulmonary vascular resistance it is larger when there is atrial fibrillation, and especially when there is mitral incompetence as well

Aneurysmal dilatation of the left atrium is more common with mitral incompetence, but it can occur with pure stenosis The left atrial appendage may be enlarged disproportionately to the rest of the chamber in such cases there is a conspicuous bulge on the left border of the heart just below the pulmonary arc but little abnormal on the right border

Heavy calcification of the mitral valve implies considerable destruction of the valve mechanism and is therefore uncommon in cases of pure



Fig 10 1 —Skiagram showing the charac terist c appea nces of dilatat on of the left atrium in the anterior view n a case of mitral stenosis



Fig 10 13—Skiagram in first oblique posi tion showing enlarged left atr um del neated by means of barium in the œsophagus in a case of m tral stenosis

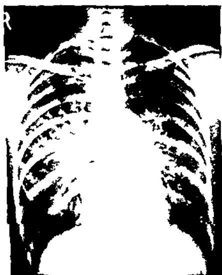


Fig 10 14—Skiagram from a case of tight mitral stenosis sho i ng intense pulmonary venous congestion (probably ch oni inter stit l œdema) Horizontal Kerley lines can be seen in the right lo er zone Dilatation of the pulmonary artery is due to passive pul monary hypertension

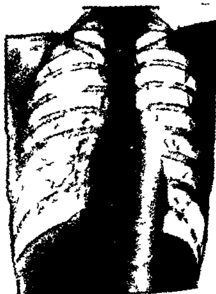
stenosis, on the other hand it does not necessarily mean that incompetence is dominant

Pulmonary venous congestion is supposed to be visible radiologically as fan shaped mottling in the hilar regions (fig 10 14) This traditional term has the advantage of familiarity but the disadvantage of inaccuracy, for the pulmonary veins are not in fact congested—if congested means over crowded—and the abnormal shadows are not venous The pulmonary venous pressure is certainly raised considerably in all cases having this radiological sign but the pulmonary veins themselves are constricted rather than dilated (Holling 1951) and the pulmonary blood volume is normal at rest (Lagerlof *et al* 1949) The precise nature of the hilar opacities awaits proof, but it is now believed that they are probably caused by a combination of chronic œdema and other changes in the interstitial connective tissue engorged lymphatics and dilated pleuro hilar bronchial veins These are the effects of pulmonary venous hypertension caused by impedance to flow the bottle neck being situated at the mitral orifice The radiological appearances themselves might well be called chronic interstitial œdema of the lungs

Horizontal linear markings best seen near the costophrenic angles usually accompany the hilar opacities (Kerley 1933 1936) These are believed to represent œdematous inter lobular septa (Grainger and Hearn 1955)



(a) 11th November 1942



(b) Two days later after medical treatment

Fig 10 15—Skiagram showing acute pulmonary œdema in a case of mitral stenosis

[illegible]

In mitral stenosis (and left ventricular failure) the degree of chronic interstitial œdema if this expression may be used is directly proportional to the height of the left atrial pressure and does not occur at all until the latter is over 10 mm Hg above the sternal angle at rest It is therefore proportional to the degree of stenosis and inversely proportional to the pulmonary vascular resistance.

Acute pulmonary œdema gives rise to a typical diffuse opacity spreading outwards from the hilum towards the periphery of the lung (fig 10 15) it is always bilateral but may be more conspicuous on one side than the other The œdema is intra alveolar and the shadows may develop and disappear within a matter of minutes or hours Attacks are more likely to occur in patients with previously normal lungs than in those who already have chronic interstitial œdema as explained earlier

Pulmonary hæmosiderosis is seen in 10 per cent of moderate or severe cases of mitral stenosis. Fine or coarse miliary nodules are scattered throughout the lungs (fig 10 16) and resemble those seen sometimes in certain hæmolytic anæmias of childhood (Gumpert 1947) The lesions are closely linked with repeated hæmoptysis and develop relatively early in the course of mitral stenosis at a time when hæmorrhages are common (Laubry Lenegre and Abbas, 1948) and the pulmonary vascular resistance



Fig 10 16—Skiagram of a case of mitral stenosis showing miliary nodules in the lungs due to hæmosiderosis



Fig 10 17—Skiagram showing considerable dilatation of the pulmonary artery in a case of mitral stenosis with an extreme pulmonary vascular resistance note the absence of chronic interstitial œdema of the lung

low (Wood, 1954). The lesions represent focal accumulations of hæmosiderin in groups of adjacent alveoli with resulting fibrosis (Lendrum 1950), and are probably caused by hæmorrhages in the walls of the terminal bronchioles secondary ossification occurs occasionally (Elkeles and Glynn, 1946) Since hæmorrhages resulting from a rising pulmonary and bronchial venous pressure tend to cease spontaneously, hæmosiderosis is never progressive beyond a certain point and since the lesions represent a permanent change of structure they never regress after successful valvotomy. They have no greater significance than recurrent hæmoptysis and point unmistakably to past miliary hæmorrhages even when there has been no history of hæmoptysis

Dilatation of the pulmonary artery (fig 10 17) is due to pulmonary hypertension and its degree is proportional to the pulmonary vascular resistance (fig 10 18) Conspicuous dilatation of the pulmonary artery

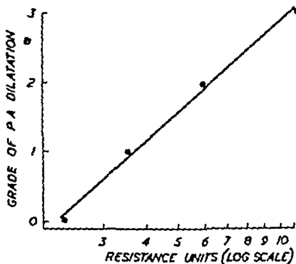


Fig 10 18—Graph showing the correlation between the radiological grade of pulmonary artery dilatation and the pulmonary vascular resistance (semi logarithmic scale)

therefore provides good evidence of at least critical stenosis for a high resistance does not otherwise develop Passive pulmonary hypertension alone is rarely severe enough to have much effect on the pulmonary artery

Enlargement of the right ventricle is more easily recognised clinically and electrocardiographically than radiologically but when the chamber responsible for cardiac enlargement has already been identified as the right ventricle by such means its actual size is best determined radiologically Like dilatation of the pulmonary artery the degree of right ventricular enlargement is proportional to the pulmonary vascular resistance and to

the duration of right ventricular failure when that has occurred Right sided enlargement is not a feature of simple mitral stenosis

Dilatation of the right atrium usually accompanies enlargement of the right ventricle and is difficult to distinguish from it by conventional radiological methods The combination of an inconspicuous pulmonary artery and dilated right heart suggests isolated enlargement of the right atrium due to tricuspid stenosis if the venous pulse and auscultatory signs deny such a diagnosis pericardial effusion should be seriously considered if that is excluded by means of cardiac catheterisation primary impairment of myocardial function due to fibrosis from old rheumatic carditis may have to be invoked although atrial fibrillation alone may be sufficient to explain some degree of dilatation

General enlargement of the heart shadow is rare in cases of mitral stenosis and when genuine is more likely to be caused by chronic pericardial effusion than rheumatic carditis or cardiac fibrosis As a rule however the statement that the heart is enlarged or that the cardio thoracic ratio is increased can be better expressed in terms of dilatation of the chamber or chambers responsible

Angiocardiography is of little value as a diagnostic tool in cases of mitral stenosis It helped however to prove that the hump on the left border of the heart between the pulmonary arc and left ventricle was the left atrium or left atrial appendage and not the conus of the right ventricle (Robb and Steinberg 1939 Grishman *et al* 1944) and that in cases with a high pulmonary vascular resistance the branches of the pulmonary arteries changed calibre abruptly and considerably instead of tapering off gradually (Davies *et al* 1953)

PHYSIOLOGICAL TESTS

Cardiac catheterisation is now chiefly employed to measure the degree of stenosis when it is doubted whether the stricture is tight enough to explain the symptoms to determine whether mitral stenosis or incompetence is dominant in difficult borderline cases in which both are obviously present, to find out whether mitral stenosis is really responsible for a situation that is clinically indistinguishable from primary pulmonary hypertension or to discover whether pericardial effusion tricuspid stenosis or a myocardial fault is causing unexplained enlargement of the heart shadow

The degree of stenosis can be estimated by measuring the left atrial pressure the cardiac output and the heart rate A simple crude index of the size of the orifice is given by the ratio of the cardiac output (L / min) to the left atrial pressure (mm Hg above the sternal angle) or C O /L A P Normally this is 5/5 or 100 per cent When mitral stenosis is trivial the index is still close to 100 per cent when the stricture is mild the index is about 5/10 or 50 per cent critical stenosis requiring valvotomy gives an average index of 4 5/22 5 or 20 per cent while with extreme stenosis th

index is about 3/25 or 12 per cent (Wood, 1954) For practical purposes this index works very well provided the heart rate does not exceed 90 beats per minute and there is no significant incompetence

The size of the mitral orifice may be calculated more accurately by taking the heart rate into consideration for forward flow through the valve can only take place in diastole According to the Gorlins (1951)

$$\text{mitral valve area} = \frac{\text{mitral flow in c c per second}}{31\sqrt{\text{L A P} - \text{diastolic L V P}}\ (\text{mm Hg})}$$

$$\text{where mitral flow (c c per sec) is } \frac{\text{cardiac output (c c per min)}}{\text{diastolic filling period (sec per min)}}$$

For example in an average case of critical stenosis with a cardiac output of 4 5 litres per minute a heart rate of 70 beats per minute and a left atrial pressure of 30 mm Hg the mitral flow in c c per second

$$\text{would be } \frac{4\,5 \times 1\,000}{35\ (\text{approx})} = 128 \text{ so that the mitral valve area would be}$$

$$\frac{128}{31\sqrt{30 - 5\ (\text{assumed})}} = 0\,83 \text{ cm}$$

Since the precise shape of the oval orifice is not known at operation it is impossible to determine its exact cross section when its length and breadth are estimated by a surgeon but it is likely to be about two third of the quotient e g an orifice measuring 1 × 0 5 cm should have a cross section of about 0 33 cm A critical orifice measuring 0 83 cm should have dimensions nearer 1 6 × 0 8 cm Thus physiological calculations based on the Gorlin formula do not tally with Brock s estimates This does not matter practically provided the order of the descrepancy is known

Obstruction to forward flow may also be demonstrated by calculating the R_{v} ratio from the left atrial pressure pulse as explained on page 113 With severe critical and mild stenosis, the ratio averages 0 6 1 0 and around 1 5 respectively This test was introduced primarily to determine whether stenosis or incompetence was dominant in borderline cases in which both were known to be present high ratios over 1 6 exclude obstruction to forward flow, so that under the clinical circumstances mitral incompetence can be diagnosed by inference

The pulmonary vascular resistance in simple units is the pulmonary arterio venous pressure gradient in mm Hg divided by the cardiac output in litres per minute as explained elsewhere In 80 per cent of cases of mitral stenosis it is normal or only slightly raised but in 12 5 per cent it lies between 0 and 10 units and in 7 5 per cent between 10 and 30 units Patients with an extreme pulmonary vascular resistance may resemble cases of primary pulmonary hypertension but cardiac catheterisation always reveals a left atrial pressure over 10 mm Hg with reference to the sternal angle a stenotic index of 10 to 25 per cent, and an R_{v} ratio under

1 3 The cardiac output is always low in these cases and the left atrial pressure strictly limited even when stenosis is extreme

The fourth reason for catheterising a case of mitral stenosis is to settle the question whether or not there is pericardial effusion, tricuspid stenosis or a myocardial fault, when apparent cardiac enlargement is otherwise unexplained

Pericardial effusion can at once be excluded if the tip of the catheter slides up and down the right border of the heart shadow when it is known to be in the right atrium If part of the heart shadow extends beyond the catheter tip as it lies against the lateral border of the right atrium however a dilated left atrium is as likely to be causing the opacity as pericardial effusion In either event dilatation of the right side of the heart without physiological cause is excluded

Tricuspid stenosis can be recognised at once if a continuous pressure tracing is recorded while the catheter is being withdrawn from the right ventricle to the right atrium for if there is any obstruction at the valve the right atrial diastolic pressure is appreciably higher than the right ventricular diastolic pressure (*vide infra*)

It is not so easy to demonstrate a myocardial fault Under routine conditions cases of primary myocardial failure associated with mitral stenosis should have a relatively low left atrial pressure perhaps 5 to 10 mm Hg above the sternal angle a more or less normal pulmonary arterio venous pressure gradient of 10 to 20 mm Hg raised right ventricular and right atrial diastolic pressures and a low cardiac output On exercise or on tipping head downwards the right ventricular and right atrial diastolic pressures should rise and the cardiac output should fall or at least fail to increase Cases that behave in this way are remarkably rare

Technically the left atrial pressure pulse on which most of the above calculations depend is recorded by wedging a catheter in a distal branch of the pulmonary artery, as described by Hellems *et al* (1948) and Lagerlof and Werko (1949) If this cannot be accomplished or if a satisfactory venous pulse is not so obtained the left atrial pressure may be measured directly by means of a needle inserted through the left bronchus (Allison and Linden, 1953), or through the chest wall posteriorly (Bjork *et al* 1953) Excellent tracings of the left atrial and left ventricular pressure pulses can of course be obtained at operation (fig 10 19)

Respiratory function tests may be required when the clinical features of a case suggest that cough and breathlessness may be due to chronic bronchitis and emphysema rather than to mitral stenosis When breathlessness is due to mitral stenosis the vital capacity and lung volume are reduced in proportion to the amount of chronic interstitial oedema present The residual volume mixing efficiency and poorly ventilated space are normal The maximum breathing capacity is diminished because of the mechanical difficulty in inflating and deflating the relatively rigid lungs the intra pleural pressure swings being greatly increased As a rule the blood gases

are normal, but in advanced cases with gross changes in the interstitial tissue there may be some difficulty in oxygen exchange as with diffuse pulmonary fibrosis The arterial oxygen saturation may then fall to 80 per cent, but rarely below this Elimination of carbon dioxide, which diffuses more readily than oxygen in a fluid medium is not hindered so that hyperventilation due to anoxia may be associated with a low arterial pCO_2 and carbon dioxide content

It will be appreciated that these findings at once distinguish the respiratory situation in mitral stenosis *from that in emphysema (q v)* In many respects however, they resemble the findings in diffuse interstitial fibrosis

The *pulmonary circulation time* is usually prolonged in well developed cases of mitral stenosis the delay being in the left atrium rather than in the pulmonary veins The test is therefore of little value because the dilated left atrium can be seen radiologically

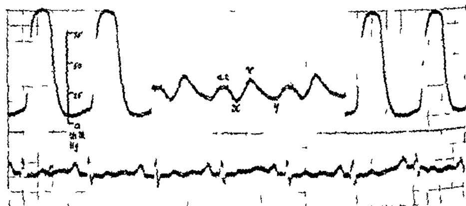


Fig 10 19 —Left ventricular and left atrial pressure pulses recorded in immediate succession from a case of mitral stenosis Note presystolic and diastolic pressure gradients across the mitral valve and the slow y descent following v

COMPLICATIONS

Strictly speaking acute pulmonary œdema hæmoptysis winter bronchitis systemic embolism, laryngeal palsy and atrial fibrillation may all be regarded as complications of mitral stenosis but for convenience they have been treated as symptoms and have already been discussed There remain pulmonary hypertension pulmonary incompetence heart failure tricuspid incompetence pulmonary embolism bacterial endocarditis and massive thrombosis of the left atrium

Pulmonary hypertension may be active or passive The latter merely serves to keep the mean pulmonary artery pressure 10 mm Hg or so above the left atrial pressure and is clinically unimportant Active pulmonary hypertension implies a high pulmonary vascular resistance and a pulmonary arterio venous pressure gradient well above normal Two grades

of active pulmonary hypertension are recognised moderate with a pulmonary vascular resistance of 6 to 10 units and extreme with a pulmonary vascular resistance between 10 and 30 units

In my own series 28 per cent of 275 critical cases of mitral stenosis developed a high resistance moderate in 16 per cent and extreme in 12 per cent The change begins early, just as the degree of stricture is becoming critical High resistances are never encountered when stenosis is mild on the other hand extreme resistances may be encountered in young adults with only average stenosis (orifice 1 × 0 5 cm) The available evidence favours the view that extreme resistances do not develop slowly over the years but relatively suddenly before pulmonary congestive symptoms have a chance to materialise It has already been explained that a high resistance protects the pulmonary venous system from developing dangerously high pressures and so prevents pulmonary œdema paroxysmal cardiac dyspnœa, and orthopnœa. On injecting 1 mg of acetylcholine into the pulmonary artery in these cases the pulmonary vascular resistance and pulmonary blood pressure fall the cardiac output rises and the left atrial pressure rises (Wood and Besterman 1956) In an ideal experiment the acetylcholine is totally inactivated before it reaches the systemic circulation and so far there has been no fall in systemic blood pressure on the contrary this has usually risen as a result of the increased output and there has been reflex cardiac slowing These results provide conclusive proof of the protective effect of pulmonary vasoconstriction on the pulmonary venous system in mitral stenosis and explain why high resistance cases do not suffer from pulmonary congestive symptoms In a carefully analysed series of 300 cases of mitral valve disease of all types 80 per cent of patients with an extreme pulmonary vascular resistance insisted that they had never had such symptoms Again if the high resistance were a late development it should be found more frequently in older patients in fact however the average age of patients with a high resistance is exactly the same as the mean age for all cases of mitral stenosis Finally, if a high resistance were due to sclerotic changes in the pulmonary arteries developing gradually over the years and secondary to passive pulmonary hypertension it should not be influenced by mitral valvotomy yet no case has so far been encountered in which the resistance did not fall appreciably after technically successful valvotomy

Just what causes the pulmonary vasoconstriction is unknown There is no experimental evidence that elevation of the pulmonary venous pressure *per se* has any such effect on the contrary the pulmonary artery pressure rises passively as it does in 80 per cent of cases of mitral stenosis Interstitial œdema can hardly excite the reflex for as previously explained these patients do not have such œdema and those that do usually have normal or only slightly raised resistances A reduced alveolar oxygen tension is known to cause pulmonary vasoconstriction but this does not occur

Clinically patients with an extreme pulmonary vascular resistance

usually present with fatigue, œdema angina pectoris or hæmoptysis from pulmonary infarction In other words the symptoms are those usually associated with a low cardiac output and not those associated with a high pulmonary venous pressure There is either a florid mitral facies and other evidence of intense peripheral vasoconstriction or rarely a palmar flush and signs of vasodilatation due to impairment of hepatic function The arterial pulse is exceptionally small The venous pressure is usually raised and the jugular pulse may show a giant *a* wave in cases with normal rhythm or a conspicuous *v* wave and deep *y* trough in cases with atrial fibrillation with or without functional tricuspid incompetence Occasionally, *y* may dominate the jugular pulse even when there is normal rhythm (fig 10 20)

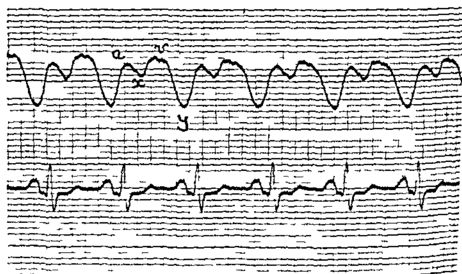


Fig 10 20—Jugular venous pulse tracing from a case of mitral stenosis with an extreme pulmonary vascular resistance and heart failure showing a rapid *y* descent and conspicuous *y* trough

The left ventricle is always impalpable but there is usually a substantial heave over the right ventricle which may extend to the left as far as the anterior axillary line occasionally there is a palpable impulse over the pulmonary artery The auscultatory signs of mitral stenosis are often greatly damped probably because the left ventricle through which they are ordinarily heard is unusually small displaced posteriorly and totally covered antero laterally by the enlarged right ventricle The mitral opening snap, however may be detected at the aortic area Right atrial gallop, a pulmonary ejection click accentuation of the pulmonary component of the second heart sound a pulmonary diastolic murmur due to functional pulmonary incompetence and a tricuspid systolic murmur due to func

tional tricuspid incompetence strongly confirms the diagnosis of severe pulmonary hypertension

The electrocardiogram shows a combined P pulmonale and P mitrale and considerable right ventricular preponderance X-rays reveal conspicuous dilatation of the pulmonary artery and right side of the heart the pulmonary interstitial and vascular markings are relatively light and the left atrium may be only slightly dilated (fig 10 17)

The physiological findings include a giant a wave in the right atrial pressure pulse when there is normal rhythm or a conspicuous v wave followed by a sharp y descent and deep y trough in cases with atrial fibrillation a left atrial pressure pulse characteristic of at least critical stenosis a pulmonary artery pressure approaching but rarely exceeding

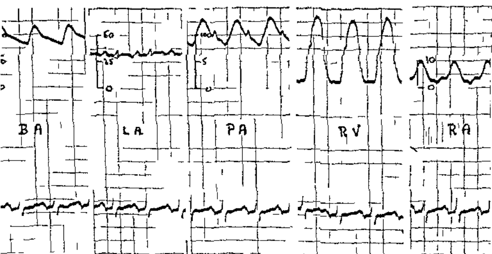


Fig 10 21—Pressure pulses from the brachial artery left atrium (indirect) and right side of the heart in a case of mitral stenosis with an extreme pulmonary vascular resistance The pulmonary artery pressure is higher than that in the brachial artery and a giant a wave is seen in the right atrial tracing

systemic level at rest (fig 10 21) a pulmonary arterio venous pressure gradient of some 30 to 70 mm Hg a high arterio venous oxygen difference associated with a low cardiac output and a pulmonary vascular resistance between 10 and 30 units (800 to 2 400 dynes sec /cm ^{5})

These high resistance cases sooner or later develop right ventricular failure and are especially prone to phlebothrombosis in the legs with secondary pulmonary embolism which is often fatal

Congestive heart failure

It has been stated more than once that uncomplicated cases of mitral stenosis with normal rhythm or controlled atrial fibrillation do not develop heart failure although they may drown from pulmonary œdema The

complication above all others that causes failure is a high pulmonary vascular resistance Thus in a consecutive series of 200 cases of mitral stenosis in which the resistance was measured there was no single instance of heart failure when the resistance was less than 7 units excluding cases with uncontrolled atrial fibrillation When the resistance was 7 to 9 5 units 50 per cent of the cases failed and when it was 10 units or over 80 per cent failed (Wood 1954) It was concluded from these unexpected findings that active carditis residual myocardial fibrosis, or any other myocardial legacy from rheumatic fever could be dismissed as a practical cause for heart failure in cases of mitral stenosis Since then however it must be admitted that rare exceptions to this general rule have been discovered

The most dangerous precipitating cause of failure in these pulmonary hypertensive cases is pulmonary embolism secondary to phlebothrombosis in the legs

The most common cause of reversible heart failure in cases of mitral stenosis is uncontrolled atrial fibrillation The very rapid ventricular rate prevents adequate left ventricular filling the cardiac output falls precipitously the renal blood flow diminishes sodium is retained and hydræmia causes œdema and raises the venous pressure at the same time the left atrial pressure rises passive pulmonary hypertension may be considerable and if the resistance is moderately raised the right ventricle may be easily overloaded impairment of myocardial function secondary to an impoverished coronary blood flow adds to the difficulties Congestive heart failure brought about in this way is far less serious than that accompanying severe pulmonary hypertension and can be corrected rapidly by controlling the ventricular rate by means of digitalis

An upper respiratory tract infection has been identified as the chief precipitating factor in 45 per cent of cases of heart failure from mitral stenosis (Werner 1936) The effect may be due to tachycardia paroxysmal atrial fibrillation or a temporarily increased pulmonary vascular resistance

Pulmonary embolism and infarction

Late hæmoptysis is usually caused by pulmonary infarction and is commonly associated with incipient or actual heart failure in high resistance cases the infarct resulting from pulmonary embolism secondary to phlebothrombosis in the legs The low cardiac output raised venous pressure and immobilisation all encourage phlebothrombosis Emboli are often recurrent, and by obstructing part of the pulmonary arterial tree increase the total pulmonary vascular resistance, so that heart failure increases and a vicious circle is established Pulmonary embolism is the commonest cause of death in this type of case Pulmonary infarction may also result from pulmonary arterial thrombosis in cases of long standing pulmonary hypertension but this is believed to be relatively rare

Pulmonary incompetence

Functional pulmonary incompetence in cases of mitral stenosis always

means a high pulmonary vascular resistance and considerable dilatation of the pulmonary artery A basal diastolic murmur associated with a relatively normal pulmonary artery and normal resistance may be safely assumed to be aortic in origin even when there is no other evidence of aortic incompetence

Tricuspid incompetence

Functional tricuspid incompetence always means considerable dilatation of the right ventricle and in cases of mitral stenosis implies a high pulmonary vascular resistance The leak is usually reversible The physical signs include a diminished x descent high amplitude *v* wave rapid y descent and deep y trough in the jugular pulse systolic pulsation of the liver and a pan systolic murmur waxing on inspiration in the tricuspid area In view of the great dilatation of the right ventricle in these cases the tricuspid murmur may be very well heard at the apex beat and may then be mistaken for the murmur of mitral incompetence

If the pulmonary vascular resistance is not high tricuspid incompetence should be regarded as organic and careful re examination is likely to disclose some evidence of stenosis for organic tricuspid lesions are rarely purely incompetent

Bacterial endocarditis

It is unusual for bacterial endocarditis to complicate established cases of mitral stenosis and only one example has been seen by the writer while studying over 500 cases of mitral valve disease during the past seven years When bacterial endocarditis involves the mitral valve the latter is nearly always incompetent

Massive thrombosis of the left atrium

Massive thrombosis occupying more than half of the left atrial cavity may be firmly adherent pedunculated or entirely free It occurs in about 2 per cent of cases of mitral stenosis (Garvin 1941) and is usually associated with atrial fibrillation The left atrium shows no special features to account for the size of the clot Free or pedunculated ball valve thrombi may block the mitral orifice and virtually halt the circulation causing sudden death or partial obstruction may result in syncope loss of peripheral pulses and severe symmetrical ischaemia of the extremities ears and tip of the nose as emphasised by Fishberg (1940) More often however the symptoms of massive thrombosis do not differ qualitatively from those of uncomplicated mitral stenosis but they may develop suddenly and tend to be severe Angina pectoris was stressed by Evans and Benson (1948) and may be attributed to the unusually low output It was hoped that angiocardiography might reveal an obvious filling defect of the left atrium in cases of massive thrombosis as it may experimentally in dogs (Read *et al* 1955) but the clot has proved difficult to demonstrate by these or other pre operative means

ASSOCIATED CONDITIONS

Pregnancy One of the most important events in the life history of a woman with mitral stenosis is pregnancy The subject is discussed in detail elsewhere It may be noted here however, that one third of all pregnancies in cases of mitral stenosis cause temporary (44 per cent) or permanent (56 per cent) deterioration The chief symptoms are cough dyspnœa hæmoptysis orthopnœa paroxysmal dyspnœa and acute pulmonary œdema atrial fibrillation systemic embolism and congestive failure are relatively rare When symptoms develop they usually begin before the end of the first trimester This tallies with physiological evidence that hydræmia and a moderate increase of cardiac output occur quite early in pregnancy, and can be demonstrated regularly during the third month (Burwell *et al* 1938 Palmer and Walker, 1949)

Anæmia usually due to iron deficiency may precipitate congestive symptoms in much the same way as pregnancy the raised cardiac output being responsible In practice the hæmoglobin is below 60 per cent and usually below 50 per cent before the output is sufficiently increased to raise the pulmonary venous pressure Before advising valvotomy therefore it is wise to check the hæmoglobin for symptoms may disappear after an iron deficiency anæmia is corrected

Thyrotoxicosis aggravates the effects of mitral stenosis by causing tachycardia and a raised cardiac output both of which are poorly tolerated as previously explained The hyperthyroidism should be corrected medically before attempting to assess the severity of the mitral stenosis if the latter requires valvotomy there is a good case for treating the goitre first by means of radio active iodine if the stricture is relatively mild the physician is at liberty to treat the thyrotoxicosis by any of the accepted methods that might seem most suitable on other grounds

Active rheumatic carditis is present in at least one third of relatively severe cases of mitral stenosis if Aschoff nodes in biopsy and post mortem material may be so interpreted The activity however is very low grade and rarely seems to influence the behaviour of the heart muscle whether or not it has any bearing on the rate at which stenosis develops or increases however is a moot point Very occasionally unexplained dilatation of the heart associated with a low cardiac output left atrial pressure under 10 mm Hg and relatively normal pulmonary vascular resistance suggests serious myocarditis or myocardial fibrosis but proof is lacking In children with established mitral stenosis there is no doubt that a recurrence of active carditis may cause reversible heart failure but fever, tachycardia and other hæmodynamic changes may be partly responsible Considering the frequency of mitral stenosis it is quite likely that some cases of unexplained heart failure associated with a relatively mild stricture are due to non rheumatic coincidental myocarditis of the type described by Gore and Saphir (1947)

Rheumatoid arthritis may be associated with mitral stenosis and may be

mistaken for a recurrence of rheumatic fever The chief cardiac complication of rheumatoid is pericarditis but a specific myocardial lesion occurs in about 2 per cent (Sokoloff 1953) Mitral valve disease is never due to rheumatoid itself

Chronic pulmonary tuberculosis occurs in about 2 per cent of cases which is the same as in the general population There is no evidence that the congested lung of mitral stenosis is antagonistic to tuberculosis

Bronchitis and emphysema have already been discussed Very rarely severe emphysema or *interstitial pulmonary fibrosis* may be incidentally associated with mitral stenosis and may be primarily responsible for breathlessness Both should be carefully considered when dyspnœa seems disproportionate to the estimated degree of stenosis It should be borne in mind that emphysema masks the auscultatory signs of mitral stenosis that rhonci may well be due to œdematous bronchial mucosa secondary to mitral stenosis, that the radiological appearances of interstitial pulmonary fibrosis can be very similar to those of chronic interstitial pulmonary œdema and that pulmonary physiology in these last two conditions can also be alike If there is any doubt about what is causing the breathlessness appropriate lung function tests should be carried out and the size of the mitral orifice calculated from data obtained at cardiac catheterisation for mistakes are certainly being made both ways patients with severe mitral stenosis being left to die in the belief that they are suffering from advanced emphysema and patients with severe interstitial pulmonary fibrosis being operated on for relatively mild mitral stenosis under the false impression that the latter is causing the dyspnœa

Essential hypertension (blood pressure 160/100 or above) occurred in only 3 per cent of the author s series and the diastolic pressure was as high as 120 mm Hg in only 1 per cent Conversely Bechgaard (1946) found that only 1 per cent of cases of essential hypertension had mitral stenosis Following valvotomy any tendency towards hypertension may become more evident

Congenital anomalies sometimes associated with congenital or acquired mitral stenosis include coarctation of the aorta patent ductus arteriosus and atrial septal defect The effects of such combined lesions on the physiology of the circulation have already been described in chapter VIII Since all are now repairable double operations may be performed if necessary

DIFFERENTIAL DIAGNOSIS

There is rarely much difficulty in recognising a case of mitral stenosis unless the characteristic physical signs are masked by a huge right ventricle or considerable emphysema the diagnostic problem is more concerned with the degree of stricture the amount of incompetence (if any) the height of the pulmonary vascular resistance the state of the myocardium the nature and degree of other valve lesions the state of the lungs and the

presence or absence of the various complications or associated conditions enumerated and discussed above No object would be achieved by commenting further on any of these things

COURSE AND PROGNOSIS

The course of mitral stenosis may be summarised here with advantage The initial rheumatic attack usually occurs between the ages of 8 and 1– The worst cases die within five years, the mortality in the active phase of the disease being 6 5 per cent The vast majority of those that recover become temporarily free from symptoms although some patients limit their activities on medical advice and others have a psychologically induced effort syndrome

The symptom free period lasts for an average of about 20 years Approximately the first half of this period is occupied with the development of physiological stenosis and is therefore a true latent interval in the second half mitral stenosis can be readily detected but the stricture is too mild to cause any symptoms Around the age of 30 true effort dyspnœa develops and usually increases a grade every 2 to 3 years so that total incapacity is reached in 7 to 8 years The steps in this relentless deterioration often appear to be sudden being precipitated by pregnancy influenza winter bronchitis the onset of atrial fibrillation a period of excessive worry or hard work or some such factor The course may also be punctuated by recurrent hæmoptysis systemic embolism acute pulmonary œdema severe bronchitis or paroxysmal atrial fibrillation

A proportion of patients die prematurely from hemiplegia or acute pulmonary œdema The development of structural changes in the interstitial tissue of the lungs helps to prolong life by allowing high left atrial pressures to be built up with relatively little danger of pulmonary œdema and the development of a high pulmonary vascular resistance may prolong life by preventing the build up of dangerously high left atrial pressures but at the expense of a low cardiac output and ultimate heart failure Patients in the first group tend to die in an attack of acute bronchitis or bronchopneumonia and those in the second group from heart failure often aggravated or precipitated by phlebothrombosis and pulmonary embolism The average duration of total incapacity is about three years so that the total period of symptoms occupies about ten years and the average age of death is about 40 There is of course a very wide variation in behaviour from case to case some patients dying in adolescence others reaching old age The figures given indicate a better prognosis than in the series reported by De Graff and Lingg (1935) in which the average age of death was 29 for cases with normal rhythm and 38 for cases with atrial fibrillation and a worse prognosis than in the follow up series analysed by Olesen (1955) in which the average age of death was 47 and the interval between the onset of symptoms and total incapacity was 15 years

TREATMENT

The management and treatment of cases of mitral stenosis is a joint concern being partly medical and partly surgical All agree theoretically that this should be so but in practice there is a growing tendency for the physician s part to be dismissed as unnecessary and time wasting so that more and more patients are being sent direct to surgical clinics It is imperative that this tendency be halted abruptly and permanently for the total physiological disturbance that results from mitral valve disease is very much a medical problem it is often thoroughly complicated and proper selection of cases for surgical treatment demands a physician s knowledge training and skill moreover there is a great deal more in the management of cases of mitral stenosis than surgical relief of the stricture fundamental and epoch making though the latter may be The physician s therapeutic responsibilities include governing the patient s total activitie steering a woman through or away from pregnancy recognising and treating important coincidental conditions such as psycho neurosis anæmia and thyrotoxicosis managing recurrent hæmoptysis preventing and treating paroxysmal cardiac dyspnœa and acute pulmonary œdema respecting and treating attacks of winter bronchitis controlling the rhythm preventing systemic and pulmonary embolism as far as possible appreciating the cause of heart failure and improving the circulation as much as possible selecting cases that require valvotomy and preparing them for the operation restoring normal rhythm post operatively accurately assessing the physiological situation three months later and guiding the patient in the most advantageous way for the rest of his medically eventful life for valvotomy does not cure rheumatic heart disease The outstanding aims of medical research workers in this field must be to prevent rheumatic fever to prevent or cure active endocarditis or at least to prevent fusion of the cusps

The patient s *work and other activities* should be regulated in accordance with the expected life history of the lesion If there is no detectable stenosis or no more than a trivial mitral leak 10 to 15 years after the initial rheumatic attack the patient should be encouraged to lead an entirely normal life If on the other hand stenosis can be detected at this time even though trivial in degree the patient should be advised to take up an occupation that will never involve him in more than light physical work so that when symptoms develop he will not have to retire During the symptom free period ordinary physical activities including all but the most strenuous competitive sports such as rowing and long distance running should be allowed on the other hand such patients must be rejected for national service and are likely to be rejected or heavily loaded by life insurance companies A woman wanting to have a family should take advantage of this latent period in which to complete it for it may be her last safe opportunity to do so At the average age of 30 or so grade 1 effort intolerance develops and progresses to grade 2A over a variable time averaging about three years During this period patients should be encouraged to continue all activities

that do not cause dyspnœa but to avoid those that do If their occupations have been chosen wisely they should have no difficulty in continuing with their work free from breathlessness Any further deterioration usually means that dyspnœa is beginning to interfere seriously with the patient s happiness and comfort and the time for valvotomy has arrived

Pregnancy precipitates or aggravates symptoms in one third of cases the deterioration being permanent in half of them If the valve lesion is obviously amenable to surgical treatment a woman with grade 1 or 2A effort intolerance should not be advised against pregnancy if she is willing to have the operation should the necessity arise If symptoms are not aggravated all is well If she deteriorates seriously she usually begins to do so in the third month and valvotomy can then be carried out if necessary the pregnancy being allowed to continue to term If the patient starts pregnancy with only grade 1 effort intolerance any exaccerbation of symptoms can usually be controlled by medical means and valvotomy is better deferred patients starting pregnancy with grade 2A effort intolerance are more likely to cause anxiety and may well require valvotomy during the second trimester Women with grade 2B effort intolerance should be advised against pregnancy unless valvotomy is carried out first if they are already pregnant valvotomy should be advised without delay If the nature of the valve lesion is such as to make surgical relief impracticable women with more than slight effort intolerance should be advised against pregnancy and preferably sterilised If she has already conceived the pregnancy is best terminated during the first three or four months by therapeutic abortion or hysterectomy if she is already five or six months pregnant and her life is not in imminent danger she can usually be taken through to term and delivered naturally symptoms being controlled by rest and appropriate medical measures Urgent hysterotomy is rarely necessary or desirable

Coincidental psycho neurosis may be entirely responsible for any disability in cases of mitral stenosis the symptoms being wholly psychosomatic or it may encourage pulmonary congestive symptoms by raising the cardiac output and heart rate This is an important diagnostic problem which must be solved correctly Effective psychotherapy is as important as curing anæmia or controlling thyrotoxicosis and should be undertaken before advising valvotomy

Coincidental anæmia may be spontaneous or secondary to repeated hæmoptysis usually the former Iron deficiency is commonly responsible and replacement therapy rapidly effective Transfusion is rarely required but packed cells may be given slowly if necessary Intravenous infusions of any kind are highly dangerous in mitral stenosis

Coincidental thyrotoxicosis is probably best treated by means of radio active iodine Mitral valvotomy can then be undertaken later if necessary Partial thyroidectomy is not without added risk in the presence of tight mitral stenosis and antithyroid drugs are unlikely to be satisfactory in the

long run In view of the bad effect of a raised cardiac output on c i c mitral valve disease it is imperative that the thyrotoxicosis h uld properly and permanently controlled

Suspected or proved rheumatic activity should be allowed to settle d before advising valvotomy when the latter is indicated but the operati should not be deferred if it is urgent There is no convincing evidence th t cortisone improves the carditis or diminishes the operation risk

Hæmoptysis from rupture of a broncho pulmonary venous radicle usu ally ceases spontaneously within a few hours If it is severe or repetitive it may be wise to lower the pulmonary venous pressure by means of rest posture mersalyl and a low sodium diet The patient should be reassured that these hæmorrhages are not serious occur relatively early in the course of mitral stenosis are not in themselves an indication for valvotomy and tend not to recur after certain natural adjustments to the circulation have taken place

Acute pulmonary œdema is a medical emergency but it is not a surgical emergency The patient should be treated sitting bolt upright with the legs down Venous tourniquets should be applied to the thighs as high up as possible Morphine gr ¼ or pethidine 100 mg should be injected intra muscularly The chief object of these measures is to lower the right ventricular output and so reduce the pulmonary venous pressure Powerful sedatives may also have some indirect influence on the permeability of the pulmonary capillaries Aminophylline 0 24 G intravenously may help by relieving bronchospasm Oxygen administered through a simple light plastic mask may help to correct the falling arterial oxygen tension and counteract the adverse effect of anoxia on the pulmonary capillary permea bility whether or not anoxia helps to bring the attack to an end by causing pulmonary vasoconstriction is not yet known for certain but a fall in alveolar oxygen tension is known to have this effect and oxygen may yet prove to be a two edged weapon

If the patient does not improve a suction catheter should be passed down the trachea via the nose or mouth in order to clear the air passages or if facilities are available bronchoscopic suction may be employed This may be life saving when a patient is drowning in fluid which is filling the air passages Finally venesection should not be unduly delayed if the occasion seems to demand it about a pint of blood should be removed

Acute pulmonary œdema can usually be prevented when its imminence is recognised by limiting physical and emotional activities (sexual inter course is a common precipitating agent) and prescribing a low sodium diet mercurial diuretics and sedatives Patients should sleep well propped up at night Respiratory infections should be treated promptly in these dangerous cases for they too may precipitate an attack Paroxysmal atrial fibrillation with a rapid ventricular rate may also be responsible and if this is suspected digitalis should be given

When the situation is under good medical control but not before valvotomy should be performed It has been well said that the patient

should not be allowed to leave hospital until the stricture has been relieved (Baker *et al* 1952)

Paroxysmal cardiac dyspnœa in which the exudation from the capillaries does not extend beyond the interstitial tissues calls for the same remedial and prophylactic treatment as acute pulmonary œdema except that intra tracheal suction is never indicated

Acute bronchitis deserves considerable respect for attacks are accom panied by much discomfort and dyspnœa and blood spitting may add to the patient s alarm Antibiotics should be supported by strong measures designed to lower the bronchial venous pressure e g posture and mercurial diuretics a low sodium diet and strict control of the ventricular rate by means of digitalis in cases with atrial fibrillation Aminophylline helps to relieve bronchospasm

The onset of paroxysmal or permanent atrial fibrillation is usually accom panied by a very rapid ventricular rate which in cases of mitral stenosis may have serious consequences as previously explained The chief dangers are acute pulmonary œdema congestive heart failure and cerebral embo lism The onset of atrial fibrillation in mitral stenosis should therefore be regarded as a medical emergency and should be treated promptly with digitalis heparin and dehydration until the ventricular rate is controlled The object of the heparin is to prevent left atrial thrombosis and 15 000 units should be given intravenously in the first instance, followed by similar doses two or three times daily intravenously or intramuscularly until digitalis is having the desired effect Prophylactic dehydration by means of mercurial diuretics and a fruit and rice diet for 48 hours help to prevent pulmonary œdema and heart failure If the patient happens to be in hospital at the time and therefore under constant supervision it may be best to give digoxin intravenously in an initial dose of 1 mg followed by 0 5 mg two hourly until the ventricular rate is under 100 beats per minute after which injections should be replaced by an oral maintenance dose A single injection of heparin intravenously and 2 ml of mersalyl intramuscularly should then suffice for the ventricular rate should be controlled within six hours If acute pulmonary œdema is present or threatened when the patient is first seen the initial intravenous dose of digoxin may be 1 5 mg but on no account more than this and subsequent doses must never exceed 0 5 mg

Permanent atrial fibrillation is best treated with a maintenance dose of digitalis attempts to restore and maintain normal rhythm being rarely worth while prior to valvotomy The matter is discussed more fully in chapter VI

Systemic embolism is due to liberation of a fresh clot from the left atrium and though usually unpredictable a limited number undoubtedly occur within a few days following the onset of atrial fibrillation with rapid ven tricular rate and these could probably be prevented by means of heparin if the danger were more widely recognised Emboli are often recurrent and

in view of their serious consequences there is something to be said in favour of treating all embolic cases with dindevan until valvotomy is performed or for life if for any reason valvotomy is contra indicated. Embolism bears little relation to the degree of mitral stricture as previously pointed out but its occurrence in otherwise uncomplicated mitral stenosis is usually sufficient reason for advising valvotomy unless the mitral index is over 45 per cent Treatment of the embolism is discussed in chapter I

Pulmonary embolism is a late manifestation of a retarded circulation in cases with a high pulmonary vascular resistance and actual or incipient heart failure In my own series this was the commonest cause of death in cases of mitral stenosis partly because the danger was not at first recognised Since treating all severe pulmonary hypertensive cases with dindevan until mitral valvotomy was carried out there have been no further deaths from this source over a period of nearly three years Prior to the adoption of this policy seven out of eight medical deaths from mitral stenosis were due to pulmonary embolism six of them in high resistance cases (Wood 1954) During the same period there was only one death from acute pulmonary œdema and that was partly the result of bronchopneumonia

If pulmonary embolism has already occurred 15 000 units of heparin should be given at once intravenously followed by adequate anticoagulant treatment for the danger of further phlebothrombosis is imminent and any delay in preventing it may be lethal There need be no fear that anticoagulants may cause serious hæmorrhage from a pulmonary infarct although hæmoptysis may be rather more prolonged The risk with which we are concerned is not hæmorrhage from an infarct but obstruction of the pulmonary circulation from recurrent embolism If mitral valvotomy cannot be carried out in this type of case because there is too much mitral incompetence the patient is too old or the operation is refused then permanent anticoagulant therapy should probably be advised

The immediate treatment of massive pulmonary embolism also includes nursing the patient flat oxygen respiratory stimulants such as aminophylline or coramine and digitalis as described in chapter XVII

Heart failure calls for complete rest preferably in a cardiac bed digitalis mercurial diuretics and a low sodium diet as detailed in chapter VII In cases of mitral stenosis it is especially important to identify the cause of the failure for it is far from being an inevitable consequence of the valve lesion The only two common causes are uncontrolled atrial fibrillation and a high pulmonary vascular resistance With the former rapid recovery follows adequate doses of digitalis alone and the subsequent outlook may then be quite good the latter is much more serious and improvement can only be temporary unless mitral valvotomy is performed

MITRAL VALVOTOMY

The treatment of mitral stenosis has been radically altered since the introduction of mitral valvotomy by Harken (1948) and Bailey (1949) in

the United States and independently by Brock (Baker Brock and Campbell 1950) in England It is true that Souttar performed the first successful digital mitral valvotomy as early as 1925 but the operation did not gain favour at that time perhaps because it was then believed that the myocardium was primarily at fault and the valve lesion relatively unimportant at that time too thoracic surgery was a formidable undertaking anæsthesia was far less advanced there were no antibiotics and there was little to encourage cardiac surgery of any kind In 1948 however the situation was radically different and mitral valvotomy was instantly acclaimed Since then thousands of cases of mitral stenosis have been relieved of their stricture and parallel physiological studies have placed the operation on a firm scientific footing The easiest and best approach is through the left atrial appendage In the simplest cases the fused commissures are separated digitally and the split is continued as far as the ring on both sides More often dense cross fusion at the critical areas of tendinous insertion have to be cut with a special knife Sometimes only one commissure can be split and occasionally the architecture of the valve is so deranged that little can be done Heavy calcification may also interfere with the operation particularly on the medial side but not necessarily Clots in the left atrium can usually be recognised by the surgeon and may often be washed out by allowing a brief frank hæmorrhage to take place through the atrial appendix a second precaution is to place tapes behind the common carotid arteries so that these vessels may be occluded for a few vital seconds when there is any danger of embolism For proper surgical details however the reader must consult appropriate surgical works

Selection of cases for valvotomy

In general any patient who is *suffering* from the effects of mitral *stenosis* requires valvotomy and any patient who is able to continue his normal occupation without distress does not There are several reasons *for not* operating prematurely (1) the surgical mortality in relatively mild uncomplicated cases is not negligible (1 7 per cent in my own series) (2) the risk of cerebral embolism at operation is not confined to advanced cases (3) a technically good result is only achieved in 75 per cent of cases and is no more likely when the stricture is relatively mild than when it is extreme (4) there is little doubt that post operative re stenosis is going to prove troublesome for it is already occurring at the rate of about 2 per cent per annum and second valvotomies are proving more difficult than the first The chief dangers of waiting until effort intolerance is grade 2B are cerebral embolism and acute pulmonary œdema, both of which may occur unexpectedly in relatively mild cases

Any patient then with simple mitral stenosis and grade 2B or greater effort intolerance should be advised to have the stricture relieved The following remarks summarise briefly the various modifying factors that have been discussed in detail previously

Age Patients under 20 years old should be deferred as long as possible in view of the likelihood of activity and the presumed greater risk of re stenosis patients in the sixth decade on the other hand should not be deferred too long for they may soon be too old for the operation

Rheumatic activity is obviously adverse but is not a contra indication if life is threatened by the stricture

Recurrent bronchitis should encourage valvotomy for it is usually the result of a high bronchial venous pressure Secondary emphysema is rarely severe enough to prevent a successful outcome

Systemic embolism is the one complication that demands valvotomy at a time that would be regarded as premature on other grounds

Hæmoptysis even when recurrent and profuse rarely provides sufficient reason for surgical intervention

Acute pulmonary œdema provides the strongest grounds for advising valvotomy as soon as intensive medical treatment has brought the situation under control

A *high pulmonary vascular resistance* may mask the severity of mitral stenosis by inhibiting pulmonary venous congestion Since the resistance is never raised unless the stenosis is at least critical valvotomy should be undertaken in all such cases When the resistance is extreme the matter is urgent owing to the grave danger of heart failure and pulmonary embolism

Atrial fibrillation has no direct bearing on the question of surgery but if it has been associated with a rapid ventricular rate breathlessness and œdema may give a false impression of the severity of the stenosis and an operation may have been advised when only digitalis is needed

Of the physical signs of uncomplicated mitral stenosis only the brevity of the interval between the aortic second sound and the opening snap and the length of the mitral diastolic murmur give any indication of the severity of the lesion The louder and sharper the first sound and the opening snap the more mobile are the mitral cusps and in such cases a good technical result may be expected from valvotomy (Sellors Bedford and Somerville 1953) Damping of the first sound and absence of the snap are usually due to heavy calcification but this should not prevent a successful outcome although only one commissure may be split

The *electrocardiogram* should show an obvious P mitrale in any case severe enough to warrant valvotomy provided the rhythm is normal Right ventricular preponderance judged by the appearances in multiple chest leads means a high pulmonary vascular resistance and therefore indicates surgical treatment

X rays are particularly helpful in showing the amount of chronic inter stitial œdema present for this is closely related to the pulmonary venous pressure and therefore to the degree of stricture Radiological evidence of pulmonary hypertension emphasises the need for valvotomy it should be remembered that in these cases signs of pulmonary venous congestion may be absent

Cardiac catheterisation should reveal a left atrial pressure well over 10 mm Hg with reference to the sternal angle a mitral stenotic index not exceeding 33 per cent and an Ry/v ratio not exceeding 1 5 average figures for surgical cases are 22 mm Hg 15 to 20 per cent and 0 8 to 1 0 respectively A high pulmonary vascular resistance, which in case of mitral stenosis always indicates valvotomy means that the pulmonary arterio venous pressure gradient is at least 30 mm Hg and the gradient divided by the cardiac output in litres per minute is at least 6 and in extreme cases at least 10 If the Gorlin formula is used the critical mitral orifice is 1 cm²

The chief difficulties in selecting cases for valvotomy however usually have less to do with the criteria and modifying factors just enumerated than with estimating the significance and degree of other valve lesions especially mitral incompetence To discuss the effect of other valve lesions on the varying physiology of mitral stenosis would entail too much repetition to be profitable for the possible permutations and combinations are almost endless Considerable experience is necessary to appreciate just what is going on in some of these complicated cases and the decision to advise or withhold mitral valvotomy can be very difficult

Pre operative treatment

Medical measures designed to diminish the operative risk and post operative complications include rest and sedatives digitalis dehydration anticoagulants and treatment of bronchitis

Rest and sedatives are advisable for a few days beforehand while the total situation is being reviewed but if unduly prolonged merely add to the patient s anxiety

Digitalis should be given as a routine whether there is normal rhythm or otherwise so that a rapid ventricular rate does not accompany post operative atrial fibrillation should that occur It is wise to start digitalis two or three weeks before valvotomy is planned so that the right maintenance dose is arrived at in good time This is not easily determined in cases with normal rhythm free from heart failure It may be best to start with tabs dig folia gr 2 t d s for two days followed by gr 1 t d s for two days followed by gr 1 twice daily thereafter This should prove *sufficient in most cases and rarely too much If nausea develops* the maintenance dose should be reduced to gr ½ t d s or 0 1 mg of digitoxin daily which is its equivalent When there is atrial fibrillation the ventricular rate must be properly controlled before valvotomy

Quinidine is not advised It has failed to prevent post operative atrial fibrillation and unless full doses of digitalis are also given it then encourages a more rapid ventricular rate slowing down the speed of the f waves so that the ventricles try to keep pace

Dehydration by means of mercurial diuretics and a low sodium diet supported or not with resins or diamox should be strictly enforced in all cases liable to acute pulmonary œdema or paroxysmal dyspnœa in all

orthopnœa cases when X rays show considerable interstitial hilar mottling and when there is heart failure secondary to a high pulmonary vascular resistance but not otherwise

Anticoagulants have already been discussed in relation to cases with an extreme pulmonary vascular resistance or recurrent systemic embolism Dicoumarol tromexan or dindevan is usually withheld four or five days before the operation

Bronchitis should be improved as much as possible before valvotomy This may mean a course of some suitable antibiotic—penicillin if the organism is believed to be the pneumococcus streptomycin if H influenzæ is responsible (May 1953)—in addition to dehydration (to lower the bronchial venous pressure) and antispasmodics such as aminophylline

Valvotomy should be deferred for several months following *hemiplegia* in view of the grave risk of post operative pulmonary complications in these cases

Post operative course and management

Immediate post operative management is a surgical responsibility and includes treatment of shock peripheral embolism hæmorrhage collapse of the lungs attending to pleural drainage and regulating fluid balance The comments made here are confined to the more medical aspects of the case

Hemiplegia occurs in about 5 per cent of cases and is always due to cerebral embolism at the time of the operation although it may not be discovered until the patient regains consciousness Subsequent embolism is extremely rare There is no effective treatment for embolic hemiplegia but spontaneous improvement may be rapid and considerable

Aortic saddle embolism or high femoral embolism is usually detected immediately if it occurs during the operation because checking all peripheral pulses is part of the surgical routine Embolectomy is always best carried out then and there

Post operative psychosis may be attributable to prolonged cardiac stand still or ventricular fibrillation during the valvotomy or to hepatic failure in patients who have had prolonged heart failure The first type is usually represented by a quietly confused soporific or comatose state the second by violently aggressive abusive or paranoid behaviour Both are serious in that they represent considerable functional damage to the cerebral cortex and liver respectively As a rule recovery is complete within a few weeks but a minority lapse into coma and death Little can be done to influence the issue

Chest complications include hæmothorax pleural effusion collapse of the lung and bronchitis or bronchopneumonia They usually settle down satisfactorily with appropriate treatment

Post operative atrial fibrillation occurs in one quarter of the cases w

previously normal rhythm This is not prevented by quinidine but causes little disturbance if prophylactic digitalis has been given It usually develops between the second and fifth day and if left to nature stops spontaneously after an average of ten days in about half the cases, and becomes permanent in the other half Attempts to restore normal rhythm at once usually fail the natural course of events indicates that quinidine should be withheld until the end of the second post operative week and if given then proves successful in 95 per cent of cases in which the valvotomy has been technically successful (Wood 1954)

Normal rhythm can also be restored in 50 per cent of patients with established pre operative atrial fibrillation but can only be maintained for long in three fifths of these

If the initial attempt to restore normal rhythm fails a second attempt may be made a few weeks later but usually without lasting success

The chief contra indications to quinidine therapy include technically unsuccessful valvotomy too much mitral incompetence extensive left atrial thrombosis and grossly diseased left atrial muscle found at operation The most important additional factor militating against prolonged maintenance of normal rhythm is advancing age

Traumatic pericarditis is believed to be responsible for the recurrent attacks of left chest pain and fever that punctuate the post operative course in 10 per cent of cases (Wood 1954) The pain is pericardial in behaviour and distribution there may be pericardial friction or radiological evidence of effusion there are often electrocardiographic changes compatible with pericarditis The fever lasts about a week and subsides without treatment After an interval of two or three weeks a second attack may occur and then perhaps a third or even a fourth Sooner or later the attacks cease for good and leave no sequelæ they are not dangerous but may interfere considerably with convalescence Similar episodes occur when a bullet or piece of shrapnel is lying in or close to the pericardium and have also been observed following direct cardiac surgery in cases of pulmonary stenosis

Heart failure following mitral valvotomy may be due to post operative sodium retention or chloride deficiency to increased mitral incompetence or to uncontrolled atrial fibrillation. An increase of pulmonary venous congestion is nearly always due to the unfortunate development of considerable mitral incompetence which is one of the risks of surgical treatment Convalescence should be very slow in these cases to give the left ventricle time to adjust itself to the changed conditions Should signs of "heart failure develop with normal serum electrolytes normal rhythm controlled atrial fibrillation and no mitral incompetence pericardial effusion should be excluded before blaming the myocardium A rare cause of post operative heart failure is pulmonary embolism

Patients are usually allowed to get up during the second week as soon as their condition warrants it and if there are no complications they may be discharged from hospital during the third week but they should remain

under close medical supervision for three months if possible and should be warned of the possibility of recurrent pericarditis

Results

In the first 260 patients operated on at the Brompton Hospital 6 9 per cent died The results were excellent in 30 per cent good in 40 per cent fair in 15 per cent and poor in 8 per cent The best cases became symptom free or if previously totally incapacitated improved to the extent of having only slight effort intolerance In other words effort intolerance changed by three grades The result was classed as good when effort intolerance changed by two grades and fair when it changed by one grade These results are more or less similar to those reported by other clinics (e g Janton Glover and O Neill 1952 Sellors Bedford and Somerville 1953 Ellis and Harken 1955)

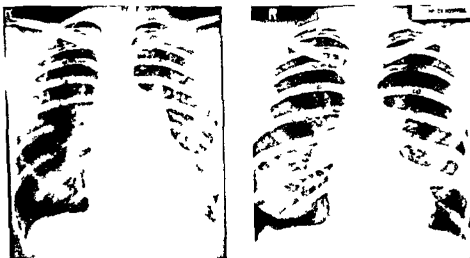


Fig 10 2—Skiagrams (a) before and (b) two years after mitral valvotomy in a case of mitral stenosis with an extreme pulmonary vascular resistance In (b) there is considerable reduction in the size of the right ventricle the pulmonary artery is less dilated and there is a gap in the left border of the heart which was previously occupied by the left atrial appendix

When the results were analysed more fully it was found that the surgical mortality in uncomplicated cases of simple mitral stenosis was only 1 7 per cent, whereas it was 33 per cent in cases with an extreme pulmonary vascular resistance 13 per cent when aortic valvotomy was carried out as well and 6 2 per cent when mitral stenosis was complicated by significant incompetence

Post operative re assessment

It has become customary to judge the results of valvotomy by the improvement in the patients effort tolerance and it has been stated repeatedly that the physical signs do not change much It must be pointed

out however that following a dramatic operation of this kind patients may become psychiatrically conditioned not to recognise cardiac symptoms and *I have more than once found a patient in frank congestive failure who* alleged that he was symptom free Objective tests of effort tolerance and physiological studies of circulatory behaviour are more reliable There is no doubt also that the physical signs may change materially when a technically successful valvotomy has been performed the presystolic murmur disappears, the first heart sound becomes far less accentuated the opening snap is distinctly late and the mitral diastolic murmur shortens considerably Radiologically pulmonary venous congestion diminishes the left ventricle may fill out and in pulmonary hypertensive cases the dilated right ventricle shrinks (fig 10 22)

Post operative cardiac catheterisation in successful cases reveals a considerable fall in left atrial and pulmonary artery pressures a rise in cardiac output a fall in pulmonary vascular resistance in cases with active pulmonary hypertension and a gratifying increase of the Ry's ratio mitral stenotic index and calculated transverse section of the mitral orifice

Subsequent course

In technically successful cases the marked improvement in effort tolerance has been well maintained in the majority of cases but relapse due to re stenosis has occurred at an approximate rate of 2 per cent per annum. In the absence of re stenosis hæmoptysis systemic embolism winter bronchitis angina pectoris pulmonary œdema paroxysmal cardiac dyspnœa and pulmonary embolism have not recurred and in pulmonary hypertensive cases congestive failure has proved reversible in those that survived the operation

Patients have been encouraged to return to work and resume active lives Subsequent pregnancies have been encouraged and have caused no trouble apart from one instance in which toxæmia caused death from acute pulmonary œdema the valve orifice at post mortem was only slightly stenosed (2 × 1 cm)

Poor or indifferent results have been due to technical failure to relieve the stricture sufficiently the production or aggravation of mitral incompetence, or the presence or development of some other factor such as a myocardial fault aortic valve disease (always more obvious after mitral valvotomy) independent bronchitis and emphysema or psychoneurosis occasionally re stenosis has occurred remarkably quickly as in the case reported by Donzelot *et al* (1953)

OTHER FORMS OF SURGICAL TREATMENT

Relief of pulmonary venous congestion has been achieved by *anastamosing the dorsal segment branch of the right inferior pulmonary vein to the azygos vein* (Bland and Sweet 1949 D Allaines *et al* 1949) and this type of operation may still have a place in cases that for one reason or another

cannot have a mitral valvotomy e g when there is too much mitral incompetence or when valvotomy has proved technically too difficult

Left atrial appendectomy was suggested as a means of preventing recurrent systemic embolism (Madden 1949) and might still be considered in cases of combined stenosis and incompetence with an unusually large atrial appendage but there is little guarantee that clots will not form in the body of the left atrium, and permanent anticoagulant therapy is probably the wiser course in these difficult cases

Ligation of the inferior vena cava has been carried out with the dual object of relieving pulmonary venous congestion or heart failure and preventing pulmonary embolism secondary to phlebothrombosis in the legs (Cossio and Perianes 1949) Although this operation has received a good deal of support in allegedly suitable cases it is not physiological and there are better ways of achieving the objects stated

AORTIC INCOMPETENCE

FREQUENCY

Rheumatic endocarditis accounts for 67 per cent of all cases of aortic regurgitation with or without stenosis syphilis being responsible for 19 per cent atherosclerosis for 7 per cent and bacterial endocarditis for 2 per cent (Campbell 1932) Congenital bicuspid or quadricuspid valve congenital hypoplasia and dilatation of the ascending aorta dissecting aneurysm trauma, and simple severe hypertension without atherosclerosis of the valve account for the remaining 5 per cent In cases of chronic rheumatic heart disease the aortic valve is involved in 44 per cent (Cabot 1926) The present account deals primarily with the rheumatic type

A good account of the history of aortic regurgitation was given by Rolleston (1940)

AGE AND SEX

About 90 per cent of cases of dominant rheumatic aortic incompetence are between 10 and 50 years of age and have had the lesion since the original rheumatic attack In Campbell s series the average age of the patients seen was 30 Males are affected twice as frequently as females

CLASSIFICATION

There are five clinical types of rheumatic aortic valve disease

1 Pure aortic incompetence
2 Aortic incompetence with trivial stenosis
3 Mixed aortic incompetence and stenosis
4 Aortic stenosis with trivial incompetence
5 Pure aortic stenosis

While this appears to be obvious it is stated for clarity and is parallel

to the five varieties of mitral valve disease Types 1 and 2 are similar physiologically as are types 4 and 5 In addition any type may be complicated by any variety of mitral or tricuspid valve disease, by any degree of myocardial dysfunction and by changes in the pulmonary vascular resistance Cases may therefore be very complex We are concerned here however with dominant aortic incompetence (type 1 or 2)

PATHOLOGY

Rheumatic inflammation of the aortic valve may cause immediate aortic incompetence Healing usually results in thickening retraction and distortion of the cusps with permanent regurgitation In addition the cusps often become adherent to one another at their bases (fusion of the commissures) so that some degree of aortic stenosis is usual Secondary calcification is common when there is stenosis

EFFECT ON FUNCTION

The stroke volume of the left ventricle is increased by an amount which is at least equal to the quantity of blood that leaks back during diastole The fibres of the left ventricle become considerably stretched in diastole the force of the heart beat is therefore augmented according to Starling's law The initial tension is increased isometric contraction is abbreviated maximum pressure is higher than normal and is attained earlier in systole the ejection phase is shortened and the pressure then falls away steeply in late systole In other words the shape of the pressure curve is altered so that early systole is loaded and late systole unloaded (Wiggers 1935) The large quantity of blood pumped so quickly and powerfully into the relaxed arteries during early systole causes an abrupt percussion wave followed by late systolic collapse The low diastolic pressure is due partly to the aortic reflux and partly to peripheral vasodilatation, the latter encourages forward flow Both add to the collapsing quality of the pulse

The cardiac output per minute remains about normal or may be even a little raised as it is in patent ductus arteriosus and arterio venous aneurysm which have much in common with aortic incompetence Effort tolerance is usually remarkably good until the disease is well advanced Sooner or later however left ventricular failure develops often suddenly and unexpectedly The heart then becomes overloaded and the output falls below normal

Zimmerman (1950) catheterised the left ventricle via the radial artery in 10 cases of aortic incompetence when there was no clinical evidence of failure (three cases) the left ventricular diastolic pressure was normal averaging 1 3 mm Hg whereas when there was congestive heart failure (seven cases) the left ventricular diastolic pressure ranged between 15 and 39 mm Hg and averaged 25 mm Hg It is hardly necessary to point out that in the absence of mitral stenosis the left ventricular diastolic pressure is the same as the left atrial diastolic pressure and can be measured accurately by more conventional methods

Experimental aortic incompetence brought about suddenly markedly reduces the efficiency of the heart After three or four months however left ventricular hypertrophy may be sufficient to compensate for the defect and work capacity may be normal If the valve lesion is then repaired the heart may be capable of performing more work than before When two cusps are injured however full compensation is never achieved (Dieckhoff 1936)

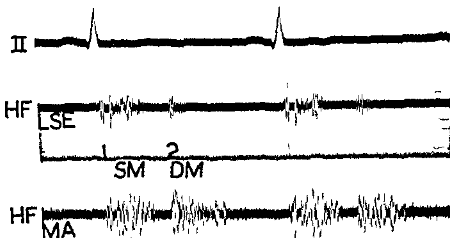


Fig 10 23—Phonocardiogram illustrating a diminuendo aortic diastolic murmur

CLINICAL FEATURES

Unlike mitral stenosis, aortic incompetence develops during the stage of active valvulitis and may be at once permanent Its early diagnosis depends entirely upon recognising an aortic diastolic murmur heard best down the left border of the sternum and closely resembling the sound of a whispered R (Hope 1839) In contrast to the mitral diastolic murmur there is little or no gap between it and the second heart sound the one passing almost imperceptibly into the other Thus the usual two beat metre of the heart sounds is not altered (fig 10 23) In distinguishing aortic from mitral diastolic murmurs the greatest stress is laid on this difference in rhythm for aortic murmurs may be heard best at the apex beat It has already been explained that owing to the appreciable period that must elapse between the closure of the aortic and the opening of the mitral valves mitral diastolic murmurs give rise to a three beat dactylic cardiac metre Only when aortic incompetence is trivial is there any clinically detectable delay in the onset of the bruit for in these cases the murmur

may only be audible when there is maximum turbulence and this may not develop until the left ventricular diastolic pressure approaches zero The appearance of the murmur phonocardiographically is then diamond shaped (Wells Rappaport and Sprague 1949) As discussed under rheumatic carditis aortic diastolic murmurs of this kind may be transient in about 20 per cent of active cases

SYMPTOMS OF ESTABLISHED AORTIC INCOMPETENCE

Effort tolerance usually remains remarkably good until the left ventricl begins to fail when breathlessness orthopnœa and paroxysmal cardiac dyspnœa develop Palpitations and throbbing however may cause dis comfort earlier Angina pectoris occurs in less than 5 per cent of cases and only when the leak is exceptionally free. Distressing attacks of pain accompanied by violent palpitations and tachycardia sometimes occur on the slightest provocation even at rest at night If the patient does not die from acute pulmonary œdema congestive heart failure sets in sooner or later sometimes it develops without clinical evidence of previous left ventricular failure as in all left sided lesions

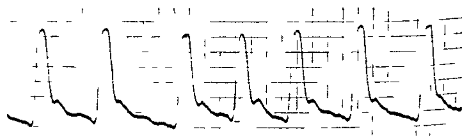


Fig 10 24—Arteriogram illustrating the water hammer pulse of aortic incompetence The percussion wave is unusually abrupt collapse precedes the pre dicrotic notch and is therefore a late systolic event

PHYSICAL SIGNS

When incompetence is well developed numerous changes in the heart and circulation may be recognised in addition to the characteristic aortic diastolic murmur Owing to enlargement of the left ventricle the apex beat is displaced downwards and to the left and the cardiac impulse is heaving and hyperdynamic At the mitral area a diastolic murmur may develop which has all the qualities of mitral origin there is a gap between its commencement and the second heart sound, it is soft, low pitched and rumbling it may be accentuated in presystole This is the Austin Flint murmur and may depend upon interference with mitral valve function by regurgitating blood It is indistinguishable from the diastolic murmur of mitral stenosis but is rarely accompanied by a thrill

During systole the increased volume of blood flung into the circulation raises the systolic pressure and distends the aorta and large arteries The upstroke of the pulse wave is abrupt and of high amplitude (fig 10 4)

When an artery is palpated this sudden shock feels like a water hammer (a Victorian toy consisting of a small quantity of fluid in a glass vacuum tube—Watson 1843) and on auscultation the sound heard may resemble a pistol shot The pulse collapses in late systole almost as quickly as it is built up, and the diastolic blood pressure is low

The abrupt distension and quick collapse of large arteries is well seen in the carotids especially when the patient sits up This characteristic visible behaviour of an artery above heart level is Corrigan's sign (Corrigan 1832)

On auscultating the femoral or other large artery a systolic murmur is heard when the vessel is compressed when a critical pressure is applied to the artery just distal to the stethoscope a diastolic murmur may also develop The latter was first described by Duroziez (1861) whose name is attached to the sign and who attributed it to retrograde blood flow during diastole Duroziez's sign may occur however in any condition causing a large primary pulse wave a steep predicrotic notch and a conspicuous dicrotic wave Such an obstacle halts the blood flow at the pre dicrotic notch but is overcome by the dicrotic wave Above the obstacle the dicrotic wave is exaggerated below it the dicrotic wave is flattened out Hence the diastolic murmur is heard above but not below the constriction The centrifugal direction of the passage of the wave which causes the murmur has been proved by means of simultaneous multiple phonoarteriograms (Luisada 1943)



Fig 10 25—Skiagram showing prominence of the aortic arch and enlargement of the left ventricle in a case of aortic incompetence

Vasodilatation exaggerates the collapsing quality of the pulse further lowers the diastolic blood pressure and causes capillary pulsation The latter may be demonstrated by lightly compressing a finger nail by transilluminating the tip of the finger or by pressing a glass slide against the lips Its presence depends upon direct transmission of the arterial pulse wave to the capillaries and it occurs in any condition in which there is sufficient relaxation of the arterioles to allow this Thus capillary pulsation may be seen in normal subjects after a hot bath in thyrotoxicosis arteriovenous aneurysm fever and in most hyperkinetic circulatory states Pulsation of the retinal veins is another common finding

Skiagrams show enlargement of the left ventricle and prominence of the aorta The ascending aorta pushes the superior vena cava further to the right the aortic knob is accentuated and the descending limb appears further to the left (fig 10 25). Unfolding of the arch is seen better in the left anterior oblique position Fluoroscopy reveals exaggerated pulsation of the left ventricle and aorta When there is left ventricular failure the usual fan shaped hilar opacities of pulmonary venous congestion develop

Electrocardiography may provide additional evidence of left ventricular enlargement (fig 10 26)

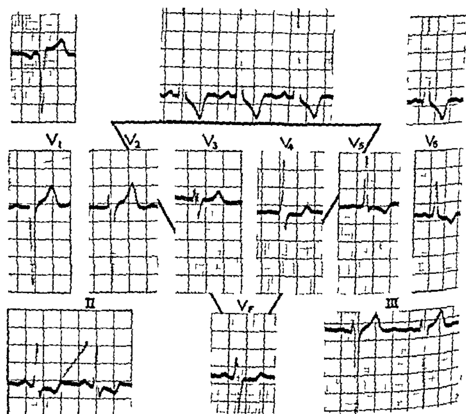


Fig 10 26—Electrocardiogram in a case of aortic incompetence showing considerable left ventricular preponderance

DIFFERENTIAL DIAGNOSIS

Most of the features described above are common to all forms of aortic incompetence

A rheumatic etiology is favoured by a rheumatic history relatively long duration any age between 10 and 40 years signs of associated aortic stenosis with or without calcification the presence of other valve lesions absence of angina pectoris, and by a normal erythrocyte sedimentation rate

It is not always easy to be certain whether the mitral valve is stenosed when the chief lesion is obviously aortic incompetence for then a mitral pre systolic or diastolic murmur backward displacement of the œsophagus and widened bifid P waves may not have their usual significance The practical point emerges that a case presenting as one of aortic incompetence with doubtful signs of mitral stenosis is better judged rheumatic on other grounds

A *spirochætal etiology* is favoured by a history of syphilis evidence of syphilis in some other system short duration age between 40 and 60 angina pectoris absence of aortic stenosis and other valve lesions calcification of the ascending aorta but not of the aortic valve irregularities in calibre of the aortic arch or frank aneurysm an accelerated erythrocyte sedimentation rate and positive Wasserman and Kahn reactions

Atherosclerosis is more likely in elderly men although some of these cases are probably rheumatic primarily Angina pectoris and some degree of calcific aortic stenosis are common in this group Aortic calcification is confined to the knuckle and valve the ascending aorta being spared The erythrocyte sedimentation rate is normal and the Wasserman reaction of course negative

Severe hypertension presents no difficulty because the aortic leak is usually trivial and does not alter the physiology of the circulation

Bacterial endocarditis should be recognised by the rapid downhill course changing murmurs and liability to perforation in addition to the fever anæmia petechiæ clubbing embolism, splenomegaly hæmaturia Osler s nodes and positive blood culture

Congenital aortic incompetence due to *anomalous cusps* alone may be suggested by the age of the patient absence of rheumatic history and the presence of some other congenital lesion *Congenital hypoplasia of the ascending aorta* with aortic ring dilatation may be part of Marfan s syndrome (arachnodactyly) The leak in these cases may be gross Congenital aortic incompetence associated with *coarctation of the aorta or ventricular septal defect* should be obvious enough

Dissecting aneurysm with survival may result in severe aortic incompetence many of these cases have been mistaken for syphilis in view of the age of the patient short duration free leak absence of rheumatic history absence of stenosis and perhaps fusiform dilatation of the ascending aorta

COURSE AND PROGNOSIS

The average life expectancy of rheumatic aortic incompetence is 20 to 30 years from its development Progno is should be based on the size of the left ventricle and upon the degree of incompetence as judged by peripheral vascular behaviour Effort tolerance often remains remarkably good until near the end Failure is commonly with normal rhythm and is usually left ventricular at first Complications are practically limited to bacterial endocarditis

TREATMENT

Medical care is a matter of guiding the patient in his choice of occupation limiting physical activities wisely but not unnecessarily steering a woman through or away from pregnancy, protecting the patient from bacterial endocarditis by the judicious use of prophylactic penicillin and treating heart failure by means of all the usual remedies when it arises Although trinitrin might be expected to aggravate rather than relieve angina pectoris in fact it proves beneficial more often than not, presumably by having a relatively selective action on the coronary circulation

Patients with aortic incompetence should be rejected for National Service and are usually rejected for insurance

Surgical treatment has so far proved unsatisfactory although Hufnagel (1954) has devised a polythene ball valve which he inserts in the descending aorta below the left subclavian artery This is said to prevent about 75 per cent of the regurgitant flow Of the first 23 cases so treated there were 17 survivors all said to be greatly improved The valve makes a considerable noise especially during the first few weeks but patients usually become accustomed to it Several cases have developed serious embolism in the legs following this operation and a small number of post operative physiological studies have revealed little if any improvement in left ventricular diastolic pressure or cardiac output The attempt to relieve aortic incompetence by surgical means however must be encouraged and better means of correcting this simple mechanical fault will no doubt be devised in due course

AORTIC STENOSIS

FREQUENCY

Aortic stenosis may be congenital rheumatic or possibly purely sclerotic The frequency of rheumatic aortic stenosis partly depends on whether cases of calcific aortic stenosis in elderly subjects without a history of rheumatic fever are regarded as rheumatic or sclerotic This point has been debated for at least half a century ever since Monckeberg (1904) recognised histologically both an inflammatory and a purely sclerotic form of stricture Both macroscopic and microscopic differences between the two have been demonstrated since by many workers e g Sohval and Gross (1936) but it is by no means easy to be sure of the initial etiology when confronted by a grossly distorted and heavily calcified valve and the alleged differences are none too convincing Two painstaking pathological studies each of 200 cases of calcific aortic stenosis were those by Clawson Noble and Lufkin (1938) and Karsner and Koletsky (1947) both teams concluded that all cases were probably rheumatic Assuming this to be so rheumatic aortic stenosis is common and must occur in at least one quarter of all cases of chronic rheumatic heart disease

PATHOLOGY

Fibrous scar tissue representing healed aortic valvulitis usually causes fusion of the cusps at their commissures Slight narrowing at the aortic aperture is thus found in most cases of rheumatic aortic valve disease When fusion extends further up the margins of the cusps true stenosis results Valve leaflets become thick rigid distorted and often unrecognisable Secondary valve calcification is common (The aorta and large arteries often remain remarkably free from atheroma (Clawson *et al* 1938) and both the frequency and severity of coronary atherosclerosis are inversely proportional to the degree of stenosis) (Dry and Willius 1939) The left ventricle hypertrophies and may finally become enormous, in a case reported by Lowe and Bate (1948) the heart weighed 2 340 G

EFFECT ON FUNCTION

The aortic orifice must be reduced to about one quarter of its natural size before changes in the circulation can be demonstrated (Wiggers 1935) Left ventricular pressure curves then show a raised initial tension steep isometric pressure gradient and an elevated maximum pressure that is reached relatively early in systole but there is no collapse as in aortic incompetence Pressure curves obtained from the aorta show an initial relatively steep rise interrupted by an anacrotic notch and followed by a slower rise that reaches its maximum late in systole the maximum pressure attained is less than normal (fig 10 27) The more severe the stenosis the earlier the anacrotic notch The ejection phase is prolonged

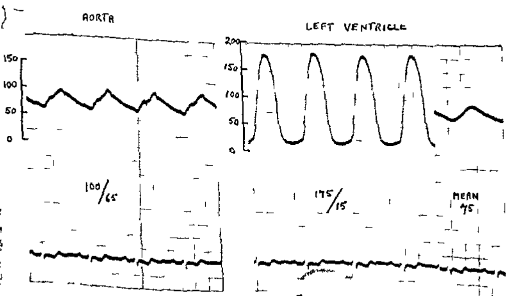


Fig 10 27—Pressure pulses from the aorta and left ventricle ... pressure gradient of 75 mm Hg Note the anacrotic notch ... stenosis showing a systolic ... summit in the aortic pulse

The systolic pressure gradient between left ventricle and aorta may be anything between a few mm Hg and over 150 mm Hg according to the severity of the stricture and the integrity of the left ventricular myocardium With a gradient of only 5 mm Hg in mild cases or in cases of mixed stenosis and incompetence the aortic pulse may still show an anacrotic notch and slow secondary rise (fig 10 28)

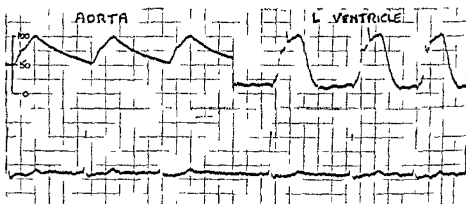


Fig 10 28—Pressure pulses from the aorta and left ventricle in a case of aortic stenosis and incompetence The pressure gradient is less than 5 mm Hg but the aortic pulse is stenotic in form

To maintain the stroke volume and cardiac output great power must be developed by the left ventricle The chamber is more hypertrophied and less dilated than in aortic incompetence Its increased initial tension is partly due to more forceful left atrial systole the left ventricle is deprived of this important help in cases of coincident mitral stenosis

The cardiac output per minute is strictly limited as in mitral pulmonary and tricuspid stenosis and in severe cases is reduced at rest The low mean aortic pressure prevents the coronary blood flow from keeping pace with the increased demands of the left ventricle

CLINICAL FEATURES

Sex and Age

Aortic stenosis is at least twice as common in men as in women The lesion may be discovered at any time from adolescence to old age usually in the sixth decade Female patients tend to be younger than male

Symptoms

Patients with aortic stenosis may complain of syncope (10–20 per cent) angina pectoris (20–36 per cent) or symptoms referabe to left ventricular or congestive heart failure (Contratto and Levine 1937 Mitchell *et al* 1954)

Syncope is of two kinds cardiac and vasomotor. Cardiac syncope is abrupt and fleeting and when it occurs on effort may be due to acute left ventricular failure or to a fixed low cardiac output so that the blood pressure cannot be maintained when peripheral vasodilatation occurs. Cardiac syncope at rest may be due to paroxysmal ventricular fibrillation or possibly to locking of the valve (de Veer 1938). Such attacks herald sudden death from a similar mechanism. The low blood pressure of aortic stenosis predisposes to vasomotor and orthostatic syncope.

Angina pectoris depends upon poor coronary filling due to the low mean blood pressure and low fixed cardiac output on effort the heavy demands of the hypertrophied and overworking left ventricle have little chance of being adequately met. The pain is indistinguishable in site quality duration and behaviour to that associated with occlusive coronary athero sclerosis and may finally occur on the slightest effort or even at rest as in advanced coronary disease.

Breathlessness on effort is of course the commonest symptom and sooner or later orthopnœa paroxysmal cardiac dyspnœa or acute pulmonary œdema may occur as a result of left ventricular failure. Œdema due to congestive heart failure may occur later or may develop without previous evidence of left sided failure as in hypertensive heart disease.

The physical signs are as follows

1 There is sometimes a delicate pale pink complexion – the Dresden china look.

2 The pulse is characteristic when relatively slow (fig 10 29) being small and sustained (plateau or slow rising pulse). It depends upon the longer duration of left ventricular systole the low blood pressure and upon the delayed development of maximum aortic pressure. These features tend

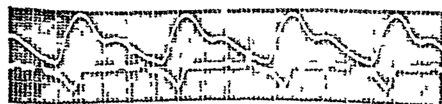


Fig 10 29.—Arteriogram in a case of aortic stenosis. The percussion wave is prolonged and the maximum pressure is reached late in systole. The photocardiogram above shows a typical mid systolic murmur

(By courtesy of Dr Frank Gardner and Max Zoob)

to disappear as the heart rate quickens The anacrotic notch of the aortic tracing may or may not be felt at the periphery for it tends to be ironed out by the elasticity of the arteries (fig 10 30) When aortic incompetence is present as well the pulse assumes a bisferiens quality (fig 10 31) To the palpating finger it feels double and may even be mistaken for coupling

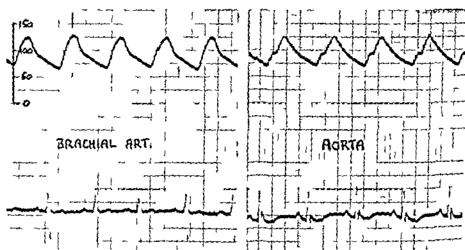


Fig 10 30—Pressure pulse from the brachial artery and aorta in a case of aortic stenosis showing disappearance of the anacrotic notch in the more peripheral tracing

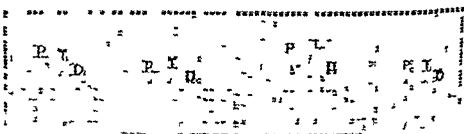
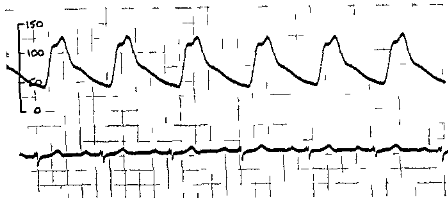


Fig 10 31—Arteriogram illustrating pulsus bisferiens in a case of combined aortic stenosis and incompetence P is the percussion wave T the tidal wave both are systolic events (B) ... J D ... F ... Gardner ... d Ma Zoob)

due to premature ectopic beats Both waves occur during the ejection phase According to Bramwell (1937) the second impulse is tidal in nature being due to overlapping and partial fusion between a forcible but prolonged percussion wave and its reflection from the periphery Aortic incompetence increases the force of the percussion wave aortic stenosis prolongs it Neither alone will produce this pulse Direct intra arterial pressure tracings show a plateau rather than a dip following the percussion wave and preceding the tidal wave (fig 10 32) The discrepancy may be due to the fact that both the palpating finger and any type of tambour used for



10 32—D rect arteriogram from a case of aortic stenosis and incompetence sho ing au instead of a dip between percu sion and tidal wa es Clinically this was a classical pulsus b sferiens

ding arterial pulsation from without must apply suitable pressure on rtery usually approximating the diastolic pressure both finger and our move through distances proportional to the pulse pressure so they record the sudden halting of the percussion wave as a negative ure for they have upward momentum at the time

The blood pressure is variable In severe cases it is low and the pulse ure small but in mild or moderate cases or when there is recognisable aortic incompetence it may be elevated and the pulse pressure may be increased About 10 per cent are truly hypertensive—an incidence a good deal lower than in controls of the same age group

4 The apex beat is displaced downwards and to the left and the cardiac impulse is quietly heaving The left ventricle is hypertrophied rather than dilated

5 A basal systolic thrill is usually present It is best appreciated when the patient leans forward and stops breathing in full expiration It may be most intense either to the right or left of the sternum A systolic thrill may also be felt over the carotid or subclavian arteries Although such a thrill is not diagnostic of aortic stenosis it is suggestive and encourages prolonged search at the base

6 A rough basal systolic murmur is almost invariable It is conducted into the cervical arteries and may be heard remarkably well at the apex beat over the left ventricle The murmur is mid systolic (fig 10 29) starting when the aortic valve opens at the end of the period of isometric contraction and finishing in physiological protodiastole when the left ventricle begins to relax appreciably before the aortic second sound (Leatham 1951) When best heard at the apex beat its timing at once distinguishes it from the pan systolic murmur of mitral incompetence When best heard at the base an aortic systolic murmur may be distin guished from a pulmonary murmur not only by its shorter duration but

also by its delayed return after the Valsalva manœuvre (Zinsser and Kay, 1950).)

7 An aortic systolic ejection click immediately precedes the murmur in many cases (Lian and Welti 1937) When heard at the apex beat this click may be mistaken for the first heart sound, and the real first heart sound for presystolic left atrial gallop the murmur is then erroneously believed to be early systolic and a diagnosis of incipient left ventricular failure with functional mitral incompetence may be wrongly made

8 The aortic component of the second heart sound is characteristically delayed in the majority of cases and absent in a minority the delay is attributed to prolongation of left ventricular systole and to the time occupied by the relaxing left ventricle in abolishing the systolic pressure gradient across the valve an absent aortic second sound is due to almost complete immobilisation of a heavily calcified rigid valve These changes result in a single second heart sound the aortic element being synchronous with the pulmonary or absent altogether or in reversed splitting of the second heart sound the aortic component falling after the pulmonary so that the split widens during expiration instead of during inspiration (Leatham 1952)) When the second heart sound is single the two components are probably fused if the sound can be heard at the apex beat and over the right carotid artery if the single second sound can be heard only at the pulmonary area the aortic component is probably absent



Fig 10 33—Skiagram of a case of aortic stenosis showing great enlargement of the left ventricle slight prominence of the ascending aorta and hilar congestion

9 On fluoroscopy the left ventricle looks dense and bulky The aorta may be conspicuous or relatively hypoplasic (fig 10 33) Post stenotic dilatation of the ascending aorta is usually more obvious at operation than in skiagrams because the shadow of the aortic root tends to merge with that of the ventricles and right atrium When the lower part of the ascending aorta is conspicuous however and the rest of it inconspicuous the presence of aortic stenosis is strongly confirmed Calcification of the aortic valve can be seen in most cases particularly if the patient is over 50

10 The electrocardiogram usually provides convincing

evidence of left ventricular enlargement Perhaps owing to the concentric type of hypertrophy and to the lack of dilatation the heart is often electrically vertical Standard leads then show the concordant pattern of left ventricular preponderance (fig 10 34) Exceptionally high voltage R waves are characteristic of aortic stenosis T is frequently inverted in leads facing the surface of the left ventricle Left bundle branch block varying degrees of atrioventricular block and atrial fibrillation each occur in about 10 per cent of cases (Mitchell *et al* 1954)

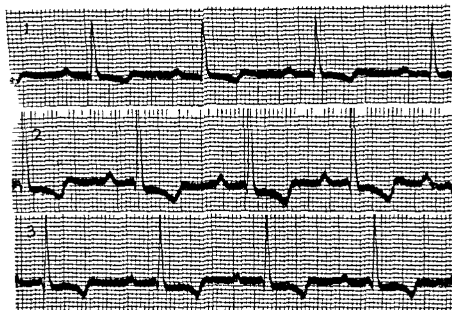


Fig 10 34—Electrocardiogram in a case of aortic stenosis showing concordant left ventricular preponderance in standard leads the heart being vertical

SPECIAL TESTS

Indirect or direct arteriograms of the brachial pressure pulse confirm the anacrotic or bisferiens pulse that is felt In doubtful cases these tracings may be helpful A normal brachial pressure pulse occupies about 0 16 seconds from its onset to the beginning of the sharp downstroke the initial upstroke or front of the percussion wave measuring 0 08 second and the blunt peak also 0 08 second In aortic stenosis the front of the percussion wave occupies 0 08 to 0 12 second to the anacrotic notch (fig 10 32) or to the beginning of the blunt peak if the notch is ironed out (fig 10 30), and the blunt peak itself occupies about 0 12 second so that from its onset to the beginning of the sharp downstroke the pulse occupies at least 0 20 second and usually 0 24 second

If the pulsus bisferiens dominant aortic stenosis is favoured if the tidal wave is taller than the percussion wave dominant aortic incompetence if it is the other way about (fig 10 35)

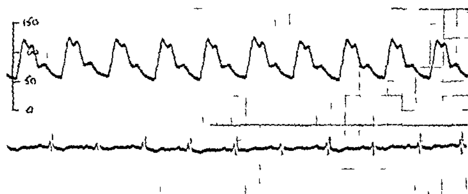


Fig 10 35—Direct arterial tracing illustrating the pulsus bisferiens in a case of aortic stenosis and incompetence with a dominant leak the percussion wave is taller than the tidal wave

Cardiac catheterisation may be helpful in assessing the degree of co incident mitral stenosis measuring the force of left atrial systole deter mining the left ventricular diastolic pressure and estimating the cardiac output at rest and on effort

Neither a powerful *a* wave in the indirect left atrial pressure pulse nor the level of the mean left atrial pressure provides any evidence of mitral valve disease in cases of severe aortic stenosis for the former may be a manifestation of left ventricular stress and the latter the result of left ventricular failure (fig 10 36) If the left atrial pressure is raised only the Ry v ratio indicates whether the mitral valve is obstructed or not In figure 10 36 Ry/v measures at least 5 so that the high left atrial pressure is obviously due to left ventricular failure or gross mitral incompetence In figure 10 37 on the other hand Ry/v is 1 3 and the raised left atrial pressure is due to coincident mitral stenosis

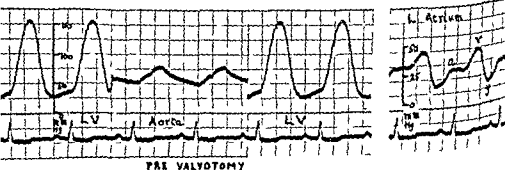
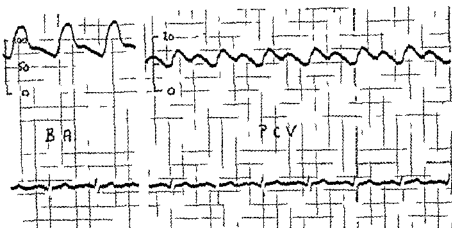


Fig 10 36—Pressure pulses from the aorta left ventricle and left atrium in a case of aortic stenosis with left ventricular failure Note the very rapid y descent and conspicuous v trough in the left atrial tracing The Ry/v ratio is 5



g 10 37—Typical wedged pulmonary artery tracing (P C V) from a case of combined rti and mitral stenosis showing an Ry v ratio of 1 3 in the indirect left atrial pressure pulse

Giant a waves in the left atrial pressure pulse have been described by orlin (1955) and are believed to be the counterpart of giant *a* waves in ne right atrium in cases of severe pulmonary stenosis Extra care may be necessary at times however to make sure that what is taken for *a* at first sight is not in fact c for accurate interpretation of wedged pulmonary artery tracings is not always easy

The *left ventricular diastolic pressure* can only be measured from direct or indirect left atrial pressure tracings when mitral stenosis can be excluded i e when the Ry/v ratio is over 1 6 A good example from a case with left ventricular failure is shown in figure 10 36 in which direct pressure tracings have been recorded from both left atrium and ventricle The raised left ventricular diastolic pressure can of course be inferred from the patient s symptoms and from the radiological appearances of the lungs

Estimation of the cardiac output at rest and on effort may be important when the severity of a case of aortic stenosis is in doubt It also provides essential data for interpreting the significance of any given pressure gradient across the aortic valve *Dye concentration curves* may be recorded with this object when the pressure gradient is being measured at operation Good outputs at rest and on effort are maintained in cases of aortic stenosis until relatively late in their course (Goldberg Bakst and Bailey 1954)

The pressure gradient across the aortic valve may be measured by recording simultaneously or in immediate succession both left ventricular and brachial pressure pulses (fig 10 36) The former may be achieved by threading a fine polythene catheter through a needle inserted directly into the left atrium from behind and manipulating it until its tip passes through the mitral valve (Bjork *et al* 1954 1955) Alternatively a needle may be passed directly into the left ventricle from the region of the apex

beat At Brompton the latter has proved safe and far less traumatic but should be undertaken only by skilled surgeons who must be prepared to carry out an immediate aortic valvotomy should ventricular fibrillation occur If the information is to be of any real value, forward flow should be measured at the same time, and if there is appreciable aortic incompetence this is impossible at the moment

Phonocardiography is of real value when the nature of the systolic murmur is in doubt when there is clinical difficulty in distinguishing left atrial gallop at the apex beat from an aortic ejection click and when the timing of aortic valve closure cannot be ascertained clinically

The *ballistocardiogram* in aortic stenosis has been studied by Van Lingen *et al* (1952) A characteristic angulated or outwardly bowed J K segment was described in tracings obtained from a low frequency critically damped instrument

Tomography is a good method of recording calcified aortic valves (Davies and Steiner 1949)

COMPLICATIONS

If syncope angina pectoris changes of rhythm left ventricular failure, congestive heart failure and heavy calcification are all regarded as manifestations of the disease itself as they should be then the only complication of rheumatic aortic stenosis is bacterial endocarditis which sooner or later occurs in about 10 per cent of cases In the large series reported by Mitchell *et al* (1954) bacterial endocarditis accounted for 20 per cent of the deaths

DIFFERENTIAL DIAGNOSIS

If as much attention were paid to the quality of the peripheral pulse as to cardiac murmurs serious aortic stenosis would be both less frequently overlooked and less often diagnosed in error nevertheless the pulse is normal in mild cases The chief sources of confusion include functional basal murmurs mitral incompetence ventricular septal defect coarctation of the aorta and a group of normotensive low output cardiopathies that may involve mainly the left ventricle such as acquired subendocardial fibrosis

Innocent basal ejection murmurs are mid systolic especially when aortic When associated with a high cardiac output as in anæmia they present little difficulty in diagnosis but when occurring alone in young persons or in association with atherosclerosis of the aorta in the elderly slight aortic stenosis is difficult to exclude A number of cases of advanced calcific aortic stenosis that have been seen in the last few years were diagnosed as having a functional systolic murmur during the first world war A similar number of young people who have this murmur at the present time are therefore being watched with considerable interest although strongly encouraged to lead normal lives

Mitral incompetence should be distinguished by the sharper quality of the pulse the hyperdynamic nature of left ventricular pulsation the

pan systolic timing of the thrill and murmur the small ascending aorta and the enlarged left atrium (As previously stated the murmur of aortic stenosis may be maximum at the apex beat over the surface of the left ventricle) When valve calcification is recognised the position of the opacity should determine whether it is aortic or mitral

Ventricular septal defect should also be distinguished by the hyper dynamic quality of ventricular pulsation and the pan systolic timing of the bruit and thrill in addition characteristic changes in the electrocardiogram and skiagram help to prevent error In doubtful cases cardiac catheterisa tion should demonstrate the shunt

Certain cardiopathies usually of unknown etiology may present with clinical electrocardiographic and radiological evidence of predominant left ventricular enlargement a low or normal blood pressure small rapid pulse and a low cardiac output (If there is a murmur it is usually apical and pan systolic being caused by functional mitral incompetence) The absence of demonstrable valve calcification may be attributed to the size and density of the heart so that the observer does not feel confident of his negative findings Cases of this sort can be awkward and diagnostic mistakes have been made in both directions (One of the sources of con usion is the belief that in about 10 per cent of cases of aortic stenosis no rtic systolic murmur can be heard at any time as reported by Bergeron *et al* (1952)) A more convincing statement would be that no *mid systolic murmur* could be heard at any time at base *or apex* by an experienced cardiologist such a statement has yet to be made In doubtful cases a phonocardiogram and intra arterial pressure tracing should be recorded and every effort made to reveal valve calcification If the diagnosis is still uncertain the pressure gradient across the aortic valve should be measured for aortic stenosis must not be missed

(In *combined aortic stenosis and incompetence* the difficulty is to decide which is dominant This is essential when selecting cases for aortic valvo tomy Since the operation was introduced it has been discovered that physiologically in mixed cases there is often more incompetence and less stenosis than traditional evidence would lead one to suppose rarely vice versa For example an obvious pulsus bisferiens seems to indicate domi nant incompetence rather than stenosis neither angina pectoris a diastolic pressure of 80 mm Hg a coarse aortic systolic thrill nor heavy valve calcification has proved reliable evidence of dominant stenosis The mixed case in fact is causing great confusion and even measuring the pressure gradient across the valve is useless without knowing the forward flow At present if a case has more than trivial aortic incompetence so that a problem does in fact arise the probability is that the leak is too great to warrant valvotomy and until more is known this may be the best attitude to adopt We have recorded pressure gradients up to 100 mm Hg across the aortic valve in cases of dominant incompetence subsequently proved at operation

Combined aortic valve disease and mitral stenosis usually presents less difficulty because the degree of mitral stricture can be worked out with precision and if this demands valvotomy then the pressure gradient across the aortic valve can be measured at operation easily enough If the mitral stenosis is relatively unimportant the problem reverts to that just discussed It may be noted here however that well developed mitral valve disease damps all the signs of aortic valve disease and these may become much more evident following mitral valvotomy

Etiological diagnosis may also be difficult Rheumatic aortic stenosis must be distinguished from congenital and calcific atherosclerotic varieties Congenital stenosis may be clinically indistinguishable from the rheumatic variety but the lesion is usually discovered in childhood there is no rheumatic history and incompetence is unusual

It is uncertain whether calcific aortic stenosis in elderly or middle aged subjects is atherosclerotic or rheumatic Thus eleven of twenty one cases reported by Christian (1931) gave a history of rheumatic fever Dry and Willius (1939) obtained a rheumatic history in 22 per cent of 228 cases and Clawson Noble and Lufkin (1938) found a rheumatic history in 35 per cent of 200 cases On the other hand in the quoted series of Dry and Willius there were 91 necropsied cases without disease of other valves a rheumatic history was obtained in only four of these—the usual incidence in any series of normal controls Again in the quoted series of Clawson and his colleagues 20 5 per cent of the patients were under 41 years of age and 39 per cent were under 51 moreover 89 had a mitral lesion as well It is obvious that many of these cases were rheumatic but this has little bearing upon the question of whether or not pure calcific aortic stenosis in elderly people is rheumatic On the pathological side Clawson (1931) particularly has drawn attention to the frequency of inflammatory stigmata of the rheumatic type but others notably Sohval and Gross (1936) have been unable to confirm such findings The best evidence of a rheumatic or other inflammatory etiology is perhaps the remarkable absence of atherosclerosis in the aorta and coronary arteries in most cases All observers have agreed on this point that these vessels must have been long protected by the stenosis However Monckeberg s original thesis that calcific aortic stenosis in elderly subjects may be degenerative (Monckeberg 1904) has not been altogether disproved

Clinically calcific aortic stenosis in elderly subjects behaves like rheumatic aortic stenosis

COURSE AND PROGNOSIS

As already mentioned the initial rheumatic attack in cases of more or less pure aortic stenosis is sub clinical in about 80 per cent of cases A mid systolic murmur however is often heard when the patient is young and well whether maximum at apex or base this murmur has usually been regarded erroneously as functional Sooner or later according to the

everity of the lesion attacks of syncope (15 per cent) or angina pectoris (33 per cent) may develop Both are serious and limit future life expectancy to an average of 3 3 and 4 1 years respectively (Mitchell *et al* 1954) Abrupt death without immediate warning presumably from ventricular fibrillation or cardiac standstill occurs in 18 per cent of severe cases Horan and Barnes 1948 Mitchell *et al* 1954) and is by no means confined to those who have had syncope or angina pectoris Subacute bacterial endocarditis may develop any time in 10 per cent of cases and accounts for 20 per cent of the deaths (Contratto and Levine 1937 Mitchell *et al* 1954) The majority of patients who survive these hazards succumb to left ventricular or congestive heart failure before reaching the age of 70 Heart failure accounted for 30 to 50 per cent of the deaths in the various series quoted above and its onset usually limits further life expectancy to 2 years

The total mortality from aortic stenosis increases in a linear manner from the third to the seventh decade (Dry and Willius 1939) after which it falls again but there are as many deaths in the eighth decade as in the sixth No distinction is made here between rheumatic and calcific aortic stenosis The average age at death is 55 to 65 women tending to be a decade younger than men

In any given case the *prognosis* varies between excellent in those with no more than an aortic systolic murmur and a life expectancy of only 2 3 or 4 years from the onset of heart failure syncope or angina pectoris respectively Between these two extremes the prognosis in symptom free cases of unmistakable aortic stenosis may be assessed by recognising three grades of severity based on the physical signs electrocardiogram and skiagram Mild cases with only slight hypertrophy of the left ventricle an aortic systolic thrill and murmur aortic ejection click and closely split or single second heart sound may be expected to remain symptom free for at least 20 to 30 years cases of moderate severity with alteration of the peripheral pulse hypertrophy of the left ventricle moderately delayed aortic valve closure grade 1 to 2 left ventricular preponderance electrocardiographically and slight enlargement of the left ventricle radiologically may be expected to live 10 to 20 years severe cases, as yet symptom free having the fully developed physical signs electrocardiogram and fluoroscopic appearances described above—particularly an unmistakable anacrotic pulse heaving left ventricle reversed splitting of the second heart sound inverted T waves in left ventricular surface leads on their equivalents and obvious enlargement of the left ventricle radiologically—cannot be expected to survive more than 5 to 10 years

TREATMENT

Medical management is similar to that of aortic incompetence Little can be done to prevent syncope other than restricting physical effort For

angina pectoris trinitrin is again of benefit more often than not, despite its theoretical objections

Aortic valvotomy (Bailey *et al* 1952) has proved more difficult and less satisfactory than mitral valvotomy The approach is through the anterior wall of the left ventricle Bailey uses a tri fin expanding dilator on a swivel head which is said to adjust itself to the commissures (Larzelere and Bailey 1953) although cinematographic demonstration of aortic valve function in cases of advanced aortic stenosis reveal so much fusion and distortion of the cusps that three commissures can rarely be made out (McMillan 1955) Simple two bladed expanding dilators may be just as effective (or ineffective)

The present high mortality of 22 per cent from aortic valvotomy (Bailey *et al* 1954) is partly due to the very advanced type of case surgeons have been invited to tackle usually those with severe angina pectoris or heart failure The physician s difficult obligation is to advise the operation in severe cases before these manifestations of impending disaster arise i e when the patient is still virtually symptom free and that is no easy matter for the risk is still appreciable and the physiological result rarely excellent

As previously stated a common mistake is to under estimate the degree of aortic incompetence present this should not be more than trivial clinically if dominant stenosis is to be confirmed surgically The error has always been in the same direction i e subsequent necropsies in cases rejected for valvotomy on the grounds of too much aortic incompetence have yet to show dominant stenosis It is repeated here for emphasis that neither angina pectoris syncope pulsus bisferiens a diastolic blood pressure of 80 to 85 mm Hg nor valve calcification can be accepted as evidence of dominant stenosis in these mixed cases even a systolic pressure gradient of 50 to 100 mm Hg across the aortic valve is inconclusive unless the forward stroke flow is known In classical cases of more or less pure severe stenosis the gradient is usually 50 to 150 mm Hg but is greatly influenced by the cardiac output at the time

So far at Brompton, 50 cases have been operated on mostly by Sir Russell Brock with a mortality of 22 per cent All these cases were advanced many far too advanced It is too early to assess the post operative results in the survivors with any precision, but it is fair to say that the best tend to be good rather than excellent and that the majority are fair rather than good (In a technically successful case a ventricular aortic pressure gradient of 50 to 100 mm Hg should be reduced to below 20 mm Hg (fig 10 38) Results of this kind are more likely to be achieved if aortic valvotomy is carried out earlier)

Combined aortic and mitral valvotomy has proved very encouraging (Likoff *et al*, 1955) It is probable that in these cases symptoms due to mitral stenosis have forced operative treatment at a time when the aortic lesion itself might have caused no symptoms at all in other words some of these cases are giving surgeons an opportunity to relieve aortic stenosis

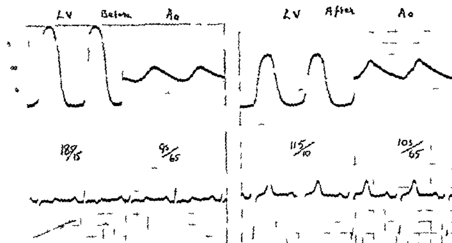


Fig 38—Pressure pulses from the left ventricle and aorta in a case of aortic stenosis before and after aortic valvotomy the pressure gradient across the aortic valve has been reduced from 90 to 10 mm Hg

when it is not too far advanced Technically most surgeons have so far preferred to undertake mitral valvotomy first, being the less hazardous of the two for ventricular fibrillation or standstill occurring during aortic valvotomy might be very difficult to correct in the presence of unrelieved mitral stenosis)

TRICUSPID INCOMPETENCE

Tricuspid incompetence may be functional or organic the former being secondary to right ventricular dilatation with expansion of the tricuspid ring as may occur in cases of pulmonary hypertension pulmonary stenosis with normal aortic root atrial or ventricular septal defect or right ventricular failure from any cause When there is pulmonary hypertension secondary to mitral stenosis clinical distinction between functional and organic tricuspid incompetence may be difficult in the first instance but the course and response to digitalis and rest may clarify the issue functional incompetence may be temporary, organic tricuspid disease is always permanent

The majority of cases of chronic rheumatic tricuspid valve disease have some degree of stenosis and the majority of cases of frank tricuspid incompetence are functional Rheumatic tricuspid disease will therefore be discussed as a whole under tricuspid stenosis and the following remarks apply chiefly to functional tricuspid incompetence

FREQUENCY

At the present time it may be unwise to attempt to assess the frequency of functional tricuspid incompetence because accurate criteria upon which

its diagnosis may be based with confidence have yet to be set up In my own cases considerable or gross tricuspid incompetence with physical signs that would be generally accepted occurred at one time or another in 22 out of 32 cases of mitral stenosis complicated by an extreme pulmonary vascular resistance (over 10 units) but in only one out of 14 cases of primary pulmonary hypertension three out of 52 cases of severe pulmonary valve stenosis with normal aortic root (R V systolic pressure over 100 mm Hg) and 10 out of 98 cases of severe atrial septal defect (pulmonary flow at least three times the systemic flow or high pulmonary vascular resistance) *This curious discrepancy was found to be due to the presence or absence of atrial fibrillation* Thus in the mitral group atrial fibrillation occurred in 62 per cent tricuspid incompetence was recognised in 91 per cent of these fibrillating cases and in only 10 per cent of those with normal rhythm In the other three groups atrial fibrillation occurred in only 8 2 per cent tricuspid incompetence was found in 87 per cent of these but in only one out of 149 cases with normal rhythm These rather startling figures make it only too clear that what is customarily taken for tricuspid incompetence is closely related to atrial fibrillation whatever the explanation may be

HÆMODYNAMICS

The effect of tricuspid incompetence on right ventricular output and filling and on the right atrial and systemic venous pressure pulse is similar in all respects to the effect of mitral incompetence on the left side of the heart and pulmonary venous circulation Functional tricuspid incompetence occurs when the right ventricle and tricuspid ring dilate as a result of failure or a physiological situation close to failure This results in initial diminution of forward flow by the amount of blood that regurgitates during systole The larger volume of blood in the right atrium however increases the pressure of the *v* wave so that when the right ventricle relaxes it is subjected to a higher filling pressure than before and dilates further to accommodate the extra blood In this sense augmented diastolic filling compensates for the leak The increased right ventricular dilatation however may cause a greater degree of tricuspid incompetence so that a vicious circle may become established forces acting in the opposite direction are myocardial resistance to unlimited diastolic stretch and the restraining influence of the pericardium so that the situation is quickly stabilised

The right atrial pressure pulse is similar to the left atrial pressure pulse in cases of mitral incompetence and is characterised by an unusually large *v* wave followed by a rapid *y* descent and deep *y* trough (fig 10 39) The 'overshoot in the early part of the right ventricular diastolic pressure tracing slightly precedes the *y* descent there being a strong potential pressure gradient from atrium to ventricle as the pressure within the latter falls rapidly to zero These appearances are identical with those found in

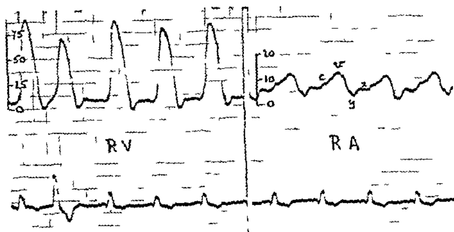


Fig 10 39—R V and R A pressure pulses from a case of severe pulmonary valve stenosis with functional tricuspid incompetence There is 2–1 atrial flutter (not well shown) and right B B B Note the absence of the x descent the steep y descent and the conspicuous y trough in the R A tracing and the so called overshoot in the R V tracing

cases of Pick s disease when the likelihood of tricuspid incompetence seems remote In the illustration shown there is 2–1 atrial flutter (not well seen in the electrocardiographic lead recorded) and right bundle branch block The *x* descent is absent as in most cases of atrial fibrillation (or flutter) just as it is in left atrial pressure tracings in cases of atrial fibrillation even when it is known for certain that there is no mitral incompetence Since nearly all cases of functional tricuspid incompetence that are recognised as such have atrial fibrillation disappearance of the *x* descent does *not* provide convincing evidence of the diagnosis despite traditional belief to the contrary Certainly the magnitude of *v* can be so great in florid cases of tricuspid incompetence as to be hard to reconcile with any other diagnosis but that is another matter Certainly all cases of tricuspid incompetence with normal rhythm and with jugular pulses having two crests and two troughs (*a* *x* *v* and *y*) are being overlooked For current expressions of the other view based on careful physiological studies the reader is referred to papers by Bloomfield *et al* (1946) Muller and Shillingford (1954) and Korner and Shillingford (1954)

CLINICAL FEATURES

Age and *sex* are related to the underlying disease not to the tricuspid incompetence

The only *symptoms* that are directly attributable to the leak are venous throbbing in the neck and abdomen swelling of the abdomen from gross enlargement of the liver and perhaps ascites and œdema although these are partly due to the primary disease tricuspid incompetence however

diminishes the cardiac output further In very advanced cases there may be impairment of hepatic function and hepatic psychosis

The *physical signs* include an unusually large *v* wave in the jugular pulse followed by a rapid *y* descent and conspicuous *y* trough (fig 10 40)

Fig 10 40—Jugular phlebogram showing fusion of the *c* and *v* waves in a case of tricuspid incompetence owing to atrial fibrillation the *a* wave is absent
(*By ... f D M x Zoob*)

systolic pulsation of the liver synchronous with the large *v* wave, occasionally systolic pulsation of peripheral veins also (when the venous valves have become incompetent) a hyperdynamic right ventricular thrust a pansystolic murmur (with or without a thrill) that waxes during inspiration and which may be heard anywhere over the distended right ventricle from the left sternal edge to the apex beat (usually formed by the right ventricle in these cases) and sometimes a short functional tricuspid diastolic murmur as well

The great majority of recognised cases are associated with atrial fibrillation as previously pointed out and either because of this or because

Fig 10 41—Right ventricular and right atrial pressure pulses from a case of organic tricuspid incompetence with normal rhythm showing preservation of the *x descent* and a conspicuous *x* trough



Fig. 10.42—Skiagram showing gross dilatation of the right atrium with a blunt right cardio-phrenic angle in a case of tricuspid incompetence

TREATMENT

Bed rest and full treatment for heart failure is advisable in the first instance to see whether the tricuspid incompetence is reversible If not the patient should be allowed up and about, although treatment for heart failure should be continued

TRICUSPID STENOSIS

Although organic disease of the tricuspid valve is found at necropsy in 10 to 20 per cent of all cases of chronic rheumatic heart disease (Cooke and White 1941 Smith and Levine 1942) clinical tricuspid stenosis is infrequently recognised It is nearly always accompanied by mitral stenosis (Pitt 1909) often by aortic valve disease as well In my own analysed series of some 500 cases of rheumatic heart disease tricuspid stenosis was found in 4 per cent, since the majority of these 500 cases were catheterised and the tracings inspected carefully for the tell tale pressure gradient the frequency given is believed to be accurate

ETIOLOGY

Tricuspid stenosis is nearly always rheumatic Both disseminated lupus and argentaffinoma however may cause it and congenital cases have been reported

PATHOLOGY

The development of chronic tricuspid valve disease following active endocarditis presumably resembles the march of events in mitral disease but the end result is somewhat different in that fusion is said to result more often in a single valve curtain perforated by a central or eccentric roundish hole than in button hole stenosis Although some degree of incompetence would therefore be expected in the majority of cases physiological studies suggest that stenosis is the commoner lesion How this tallies with necropsy evidence to the contrary remains to be seen Aceves and Carral (1947) for instance found tricuspid valve disease in 33 per cent of 147 consecutive necropsies in cases of rheumatic heart disease of these 11 were stenosed 28 incompetent and 11 mixed It is possible therefore that cases of organic tricuspid incompetence are being overlooked clinically

HÆMODYNAMICS

Tricuspid stenosis tends to prevent proper filling of the right ventricle and therefore both lowers the cardiac output and relieves pulmonary venous congestion caused by mitral stenosis, which is invariably present The obstruction results in elevation of the right atrial pressure and in a presystolic (fig 10 44) or diastolic pressure gradient (fig 10 45) across the tricuspid valve, similar in all respects to the pressure gradient across the mitral valve in cases of mitral stenosis (fig 10 46) The presystolic gradient

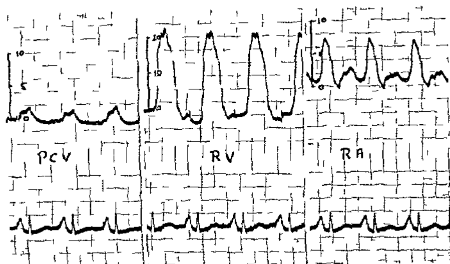


Fig 10 44—Intracardiac pressure pulses from a case of tricuspid stenosis with normal rhythm showing giant a waves in the right atrial tracing and a presystolic pressure gradient across the tricuspid valve

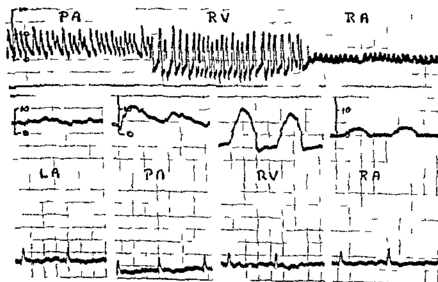


Fig 10 45—Intracardiac pressure pulses in a case of tricuspid stenosis with atrial fibrillation showing a diastolic pressure gradient across the tricuspid valve a rather slow y descent and absence of the y trough

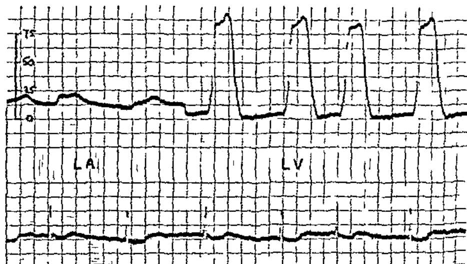
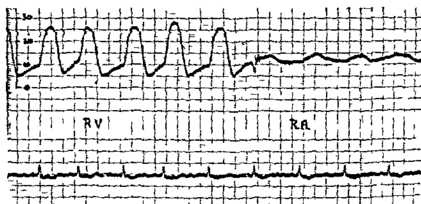
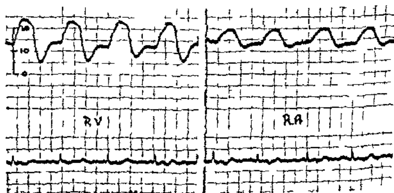


Fig 10.46—Pressure pulses from the left atrium and left ventricle in a case of mitral stenosis with atrial fibrillation showing a diastolic pressure gradient across the mitral valve slow y descent and absent y trough



Tricuspid stenosis pre operative



Post operative tricuspid incompetence

Fig 10.47—Pressure pulses from the right ventricle and right atrium in a case of tricuspid stenosis before and after tricuspid valvotomy The slow y descent and absent y trough have been abolished

is seen with normal rhythm the diastolic with atrial fibrillation Filling of the right ventricle is retarded so the rate of *y* descent following *v* in right atrial and jugular pressure pulses is relatively slow (fig 10 47) and there is no appreciable *y* trough (Gibson and Wood 1955) The change in the slope of *y* and the development of a *y* trough following surgical relief of the obstruction is well shown in the lower tracing of figure 10 47 (tricuspid incompetence was produced inadvertently in this case) The size of the orifice may be calculated from the cardiac output pressure gradient and heart rate as described for mitral stenosis

The right atrium becomes hypertrophied and distended while the right ventricle remains quiet underfilled and small The low cardiac output high venous pressure and distended liver encourage œdema and ascites as in Pick s disease, which in some respects it resembles (Thompson and Levine 1937)

CLINICAL FEATURES

There were 16 women and 6 men in my small series of 22 cases Their average age was 35 the range 21 to 48 Figures from the literature are not included because up till now the majority of mild and moderate cases have been overlooked clinically Necropsy figures however show that the average age and sex ratio in tricuspid cases is much the same as for mitral stenosis (Aceves and Carral 1947)

Symptoms

The first symptom may be fluttering discomfort in the neck caused by the development of a giant *a* wave in the jugular pulse More often the pulse is seen in the mirror or noted by an interested relative Hepatic pulsation is rarely mentioned by the patient

Apart from this there are no complaints attributable to tricuspid stenosis until the cardiac output is sufficiently reduced to cause fatigue or the liver sufficiently enlarged to cause obvious swelling of the abdomen œdema and ascites follow At the same time the patient is usually spared the distressing symptoms that would otherwise have developed on account of the associated mitral stenosis thus hæmoptysis acute pulmonary œdema paroxysmal cardiac dyspnœa orthopnœa and winter bronchitis are noticeably absent in the majority of cases

Physical signs

There are so many characteristic and specific features of tricuspid stenosis that it is remarkable how frequently the clinical diagnosis is overlooked In fact a confident bedside diagnosis can be made in 80 per cent of cases if proper attention is paid to the following points

1 If there is normal rhythm there is almost invariably a *giant a wave* in the jugular pulse (fig 10 48) and *presystolic hepatic pulsation* as noted by Mackenzie (1902)

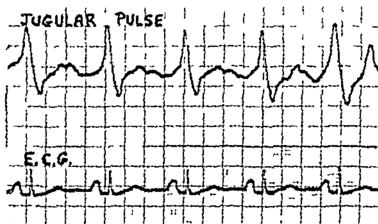


Fig 10 48—Jugular phlebogram showing giant *a* waves in a case of tricuspid stenosis with normal rhythm

2 If there is atrial fibrillation there is a prominent *v* wave in the jugular pulse which characteristically subsides slowly, *there is no y dip* (fig 10 47) as there is in all other conditions with venous pressures at this level (Owen and Wood 1955 Gibson and Wood 1955)

3 *The heart itself is quiet* there being no appreciable lift over the right ventricle as there usually is in pulmonary hypertensive cases of mitral stenosis which may also cause giant *a* waves in the jugular pulse Pulmonary valve closure is also impalpable

0·2 Sec
TA
ASM 2
ASM 2
TA
LF
JUG
LEAD II

Expiration Inspiration

Fig 10 49—Phonocardiogram showing the effect of inspiration on the tricuspid atrio-systolic murmur The prominent *a* wave in the jugular phlebogram also increases with inspiration

4 *Auscultation* at the left sternal edge in the fourth space reveals a tricuspid presystolic or diastolic murmur which is sharply accentuated during inspiration (fig 10 49) when right ventricular filling is encouraged (Carvallo 1950) A thrill may accompany the bruit A tricuspid opening snap may also be heard (Kossman 1955) but may be difficult to distinguish from the mitral opening snap which is usually present unless it is accentuated during inspiration Accentuation of the tricuspid first sound also increased by inspiration is even less convincing An associated tricuspid systolic murmur may be present but is far from invariable The pulmonary component of the second heart sound is not accentuated as in pulmonary hypertensive cases of mitral stenosis and there is never right atrial presystolic gallop which usually accompanies the giant *a* wave in other conditions

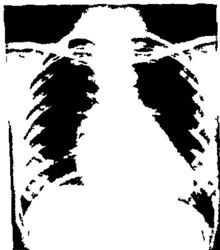


Fig 10 50—Skiagram from a case of tricuspid stenosis showing conspicuous enlargement of the right atrium without dilatation of the pulmonary artery note also the absence of pulmonary venous congestion

5 *Fluoroscopy* shows characteristic enlargement of the right atrium without conspicuous dilatation of the pulmonary artery and the lung fields are relatively clear (fig 10 50) Absence of enlargement of the right ventricle is difficult to demonstrate radiologically when the right atrium is dilated Calcification of the tricuspid valve is very rare

6 The *electrocardiogram* in cases with normal rhythm commonly shows the highly characteristic combination of an unusually tall widened P wave (combined P pulmonale and P mitrale) and absence of right ventricular preponderance (fig 10 51)

DIFFERENTIAL DIAGNOSIS

The possibility of tricuspid stenosis should be borne in mind in any case of mitral valve disease in which the jugular venous pressure is unquestionably raised the differential diagnosis then lying between this, uncontrolled atrial fibrillation severe mitral incompetence a high pulmonary vascular resistance and pericardial effusion for in uncomplicated mitral stenosis the venous pressure is nearly always normal a primary myocardial fault being rare (Wood 1954)

Digitalis soon controls the ventricular rate and allows the jugular pulse to be analysed more easily Mitral incompetence should be recognised

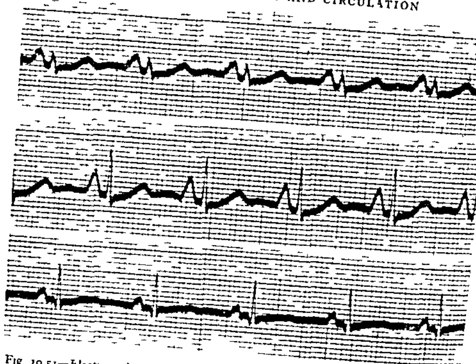


Fig 10 51—Electrocardiogram showing exceptionally tall yet widened P waves in a case of mitral and tricuspid stenosis Note also the absence of right axis deviation

without difficulty and if severe the likelihood of associated tricuspid stenosis is remote If a high pulmonary vascular resistance is responsible for the giant *a* wave it should be recognised by the heaving right ventricle accentuated pulmonary second sound conspicuously dilated pulmonary artery and strong right ventricular preponderance electrocardiographically Pericardial effusion may have to be considered but it does not cause a giant *a* wave slow *y* descent nor absent *y* trough radiologically the app arances can be similar but the P wave of the electrocardiogram is normal when there is sinus rhythm Pathognomonic of tricuspid stenosis are the slow *y* descent and tricuspid bruits

Fbstein s disease certain cardiopathies usually of unknown or uncertain etiology and chronic constrictive pericarditis may bear some superficial resemblance to rheumatic tricuspid stenosis but their distinction is rarely difficult They are more likely to be confused with isolated tricuspid stenosis from disseminated lupus

SPECIAL TESTS

Cardiac catheterisation is the most convincing way of proving or disproving the existence of physiological tricuspid stenosis By sliding the tip of a looped catheter up and down the lateral wall of the right atrium pericardial effusion can be easily diagnosed or eliminated After recording left atrial and pulmonary artery pressures and measuring the cardiac output

in the usual way the catheter is withdrawn slowly from the right ventricle to the right atrium while intracardiac pressures are recorded continuously In normal controls the diastolic and presystolic right atrial pressure is identical with the right ventricular diastolic and end diastolic pressure respectively (fig 10 52) whereas in tricuspid stenosis a presystolic or diastolic pressure gradient across the valve can be demonstrated routinely (fig 10 53 and 10 47) If by ill fortune the right ventricle cannot be entered the slow y descent in the right atrial tracing should still reveal the correct diagnosis The Ry/v ratio has not yet been worked out for tricuspid valve disease

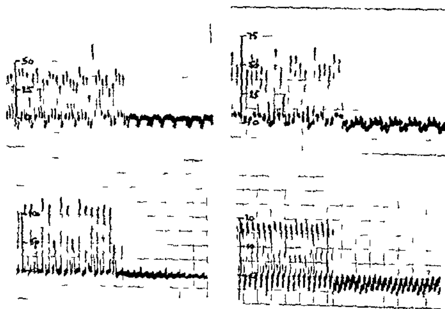


Fig 10 5 —Withdrawal tracings from right ventricle to right atrium showing identical diastolic pressures in these two chambers in four controls

Phonocardiography confirms the tricuspid origin of the murmurs and demonstrates their relationship to respiration (fig 10 49)

PROGNOSIS

It has long been known that some patients with obvious tricuspid stenosis may carry on their occupations for a remarkably long time with relatively little disability On the other hand others linger on year after year in considerable distress from fatigue chronic œdema ascites and distended abdomen whether they attempt to continue a sedentary occupation or not A rigid low sodium diet repeated injections of mersalyl and occasional abdominal paracentesis may relieve these symptoms but not without adding their own discomforts

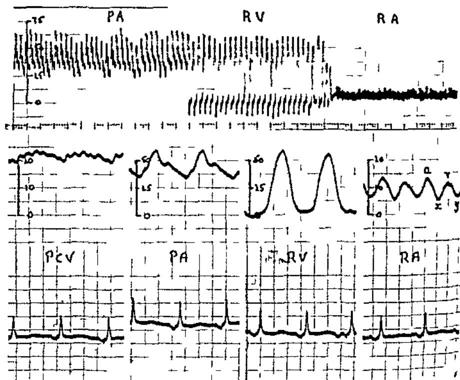


Fig 10 53—Withdrawal tracings from the right ventricle to the right atrium in a case of tricuspid stenosis with normal rhythm showing a presystolic and diastolic pressure gradient across the tricuspid valve

Aceves and Carral (1947) found that life expectancy averaged five years from the time the diagnosis was first made but in the past the diagnosis has been made notoriously late Thompson and Levine (1937) particularly have emphasised the relatively long life expectancy and surprising ability of patients to carry on despite the discomforts and gross physical signs alluded to above

TREATMENT

Medical measures include all the usual means of combating chronic ascites and œdema prior to their onset however the patient should not be unduly restricted for there is little danger of acute pulmonary congestive symptoms despite coincident mitral stenosis

Tricuspid valvotomy has only been undertaken in a few isolated cases so far (Trace *et al* 1954 Chesterman and Whittaker 1954 O Neill Janton and Glover 1954 McCord Swan and Blount, 1954) There may be considerable difficulty in locating the commissures and serious tricuspid incompetence may result from too bold an attack as in the patient whose tracings are illustrated in figure 10 47 In the great majority of my own cases the tricuspid stenosis was not severe enough to warrant interference although mitral valvotomy was carried out in several of them

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CHAPTER XI

NON-RHEUMATIC MYOCARDITIS AND MISCELLANEOUS CARDIOPATHIES

UNDER this heading are grouped together all those varieties of heart disease that have in common a primary or predominant myocardial fault That only one chapter should be devoted to what might appear to be the very essence of cardiology emphasises the curious fact that the great majority of so called diseases of the heart are simply those conditions that hinder filling mechanisms increase cardiac work or interfere with fuel supplies i e mechanical disadvantages of one kind or another What greater compliment could be paid to the general health and integrity of the myocardium itself than this?

Incidence

At present no definite figure can be given for the prevalence of non rheumatic myocarditis and clinically similar cardiopathies, for there are wide discrepancies between clinical instrumental and pathological data

However out of approximately 10 000 new patients with cardiovascular disease examined personally by the author only 30 were in this category excluding cases of diphtheria thyrotoxicosis myxœdema and digitalis or quinidine intoxication This gives a relative clinical frequency of 0 3 per cent for cases presenting like isolated myocarditis

Age and sex

The average age of the patients in this series was 44 the range 14 to 63 but a primary myocardial fault may occur at any age In infants a congenital cause such as fibroelastosis von Gierke s disease or anomalous origin of the left coronary artery from the pulmonary artery is more likely

The male/female sex ratio was 2 1

Classification

The group comprises numerous infections and infestations the collagen diseases and allied allergic states disorders of metabolism or nutrition certain endocrine disturbances neuro muscular dystrophies primary or secondary tumours of the heart and a number of drugs and poisons included also are at least two important cardiopathies of unknown origin—isolated myocarditis and endomyocardial fibrosis For convenience a list of the more important members of each sub group is given below

ETIOLOGY

Bacterial infections
1 Invasive
 Pyogenic organisms
 Syphilis
2 Toxic
 Bacterial endocarditis
 Diphtheria
 Meningococcal septicæmia
 Pneumonia
 Streptococcal infections
 Tuberculosis
 Typhoid fever
 Typhus (especially scrub typhus)

Fungus or yeast infections
Actinomycosis
Coccidioidomycosis
Histoplasmosis

Parasitic or protozoal infections
Bilharziasis
South American trypanosomiasis (Chagas disease)
Toxoplasmosis
Trichiniasis

Virus infections
Common cold
Infective mononucleosis
Influenza
Mumps
Poliomyelitis

Isolated myocarditis
Endomyocardial fibrosis
Fiedler s type

Allergic or other tissue reactions
Loffler s syndrome
Sarcoidosis

Collagen diseases
Dermatomyositis
Disseminated lupus
Periarteritis nodosa
Rheumatoid arthritis
Scleroderma

Congenital anomalies
Anomalous left coronary artery
Familial cardiomegaly
Fibroelastosis
Friedreich s disease
Gargoylism
Von Gierke s disease

Drugs
Adrenalin, Emetine
Calcium, Potassium
Digitalis, Quinidine

Endocrine disorders
Acromegaly and gigantism
Myxœdema
Thyrotoxicosis

Metabolic or nutritional disorders
Alcoholism
Amyloidosis
Beri beri
Diabetes mellitus
Hæmochromatosis
Malnutrition

Neuromuscular dystrophies
Progressive muscular dystrophy

Tumours
Fibroma
Leukæmia
Myxoma
Rhabdomyoma
Sarcoma
Secondary tumours
Argentaffinoma

Hæmodynamics

The chief physiological fault common to nearly all groups is inability on the part of the weakened myocardium to maintain an adequate cardiac output despite normal pressure and volume loads normal coronary flow and normal rhythm Hypertrophy of relatively healthy muscle fibres a high filling pressure in both venous systems giving increased diastolic stretch, and tachycardia may compensate for the defect for a while but

sooner or later prove inadequate one or other or both ventricles becoming overloaded

BACTERIAL INFECTIONS

The great majority of cases of myocarditis secondary to bacterial infection are toxic and the best example is diphtheritic myocarditis Bacteria may actually invade the myocardium however in certain instances e g in syphilitic myocarditis (q v) and suppurative myocarditis Miliary or solitary absce ses of the myocardium may occur in staphylococcal or pneumococcal septicæmia and may cause purulent pericardial effusion or cardiac rupture (Weiss and Wilkins 1937) The outlook in these previously fatal cases has altered considerably since the advent of penicillin and other antibiotics

THE HEART IN DIPHTHERIA

Diphtheria may cause peripheral circulatory collapse or toxic myo carditis Cutaneous diphtheria so easily overlooked and so often untreated until too late may be as lethal as the common faucial type Early and adequate treatment with antitoxin has greatly reduced the incidence of toxic complications but has by no means abolished them Experimentally in dogs diphtheria toxin causes peripheral vasodilatation conduction defects and weakness of myocardial contraction ending in failure (Witt Lindner and Katz 1937)

CIRCULATORY COLLAPSE

Towards the end of the first week or during the second week of the ill ness the blood pressure may fall well below 100 mm Hg the patient becomes faint sick and restless the skin pale cold and clammy the pulse rapid and thready Loss of vasomotor tone may be due to toxic depression of the vasomotor centre perhaps to peripheral sympathetic paresis, or possibly to poisoning of the vessels themselves Occasionally it is brought about by suprarenal failure due to necrosis or hæmorrhage The earlier the onset of circulatory collapse the worse the prognosis Patients usually re main in a critical state for several days in those who recover improvement may then occur but the blood pressure usually remains low for two or three weeks

The course of diphtheria may be complicated (as well as alleviated) by serum therapy for this may induce not only immediate collapse from anaphylactic shock in a sensitised individual but also later collapse from loss of plasma into the tissue spaces associated with serum sickness Urti caria and œdema usually on the ninth day may be extreme and result in a diminished blood volume and hæmoconcentration Diphtheritic circula tory collapse and allergic shock may thus be expected at about the same time and diagnostic difficulties may arise

Treatment of serum sickness includes subcutaneous adrenalin 0 5 mg two to four hourly sodium salicylate gr 15 to 20 (1 to 1 25 G) three hourly and one of the anti histamine drugs such as diphenhydramine (benadryl) 50 mg six hourly

Treatment of diphtheritic circulatory collapse consists of raising the foot of the bed and maintaining the blood pressure by means of a slow drip infusion of some suitable pressor amine such as noradrenalin, at a rate of about 5 to 15 μg per minute In view of the uncertain state of the myocardium in these cases too much saline must not be given and the blood pressure should not be raised above 120 mm Hg It is best to use a strength of 1 mg of noradrenalin to 100 ml of normal saline 15 drops (1 ml) of such a solution per minute should contain 10 μg of noradrenalin Alternatively mephentermine may be given intramuscularly in doses of 25 to 50 mg (usually 30 to 35 mg) and repeated when necessary or mephentermine may be given by slow intravenous drip at a rate of 0 5 to 1 mg per minute until the blood pressure is satisfactory

The *prognosis* is grave

TOXIC MYOCARDITIS

Pathology Diphtheritic carditis being toxic in nature may prove fatal without causing advanced changes in morbid histology The characteristic finding is hyaline degeneration or necrosis of muscle the fibres losing their striations and presenting a swollen granular appearance Lesions are patchily distributed and only short segments of individual muscle fibres may be affected Monocytes cluster round the debris and fibroblastic repair follows (Gore 1948)

Clinical features Disturbances of rhythm tend to occur first usually during the second week of the disease Partial or complete heart block and bundle branch block are the best known and in patients who recover from the illness are usually but not invariably transient (Perry, 1939) Both heart block and bundle branch block commonly denote severe carditis most such cases proving fatal (Burkhardt Eggleston and Smith 1938) Ectopic beats are common and although often innocent and unrelated to carditis should be viewed with suspicion in diphtheria Auricular fibrillation and paroxysmal tachycardia are rare Ventricular fibrillation may be responsible for sudden death

Other evidence of carditis tends to occur a little later usually during the third week Sinus tachycardia gallop rhythm enlargement of the heart and reduction of the pulse pressure are usual The onset of heart failure may be suggested by pallor breathlessness præcordial oppression and vomiting Congestion is systemic rather than pulmonary the jugular venous pressure being raised and the liver distended there is rarely orthopnœa paroxysmal cardiac dyspnœa or pulmonary œdema Significant murmurs and pericardial friction are absent

The *electrocardiogram* is especially helpful in the diagnosis of diphtheritic carditis much more so than in rheumatic carditis Depression of the RS T segment or primary inversion of the T wave in most leads is characteristic and is found during the second week in the majority of cases which develop clinical carditis and in some that do not A similar pattern may be produced in cats within 48 hours by injecting diphtheritic toxin (Nathanson 1928) Of 600 cases of diphtheria studied by Altshuler *et al* (1948) 108 or 18 per cent developed these changes while only 11 showed heart block

Radiological studies on diphtheritic carditis are rare because patients are not allowed to stand or sit, and should not be moved to the X ray department Portable skiagrams give little information about the size of the heart General dilatation however may be expected if the venous pressure is raised

Prognosis The outlook is grave for sudden death is common and presumably results from ventricular fibrillation or asystole Some patients die from congestive heart failure Not infrequently associated circulatory failure complicates the picture Those who survive usually develop polyneuritis later and this is apt to be severe The total mortality rate is difficult to assess for mild cases may well be overlooked but it is usually put at 50 per cent

If the patient survives the ultimate prognosis is excellent (White *et al* 1937) and complete recovery may be promised without reserve It is important that the patient should be convinced of this from the start in order to prevent anxiety neurosis and to maintain good morale

Treatment Antitoxic serum will already have been administered in most cases if not it is too late to give it by the time cardiovascular symptoms develop The axiom that antitoxin cannot do any harm and might as well be given even at this stage is untrue for serum reactions are common and may prove fatal when there is toxic circulatory collapse or carditis

Prophylactic treatment in addition to early and adequate doses of antitoxin consists of complete rest in bed for a minimum period of one month in all cases of diphtheria If by the end of this time there is no evidence of cardiovascular or neuro intoxication there is little further risk to life Should any such intoxication have occurred however bed rest must be extended for another month otherwise sudden death may occur during convalescence in the second month Patients may be treated with far less respect subsequently even when they have extensive polyneuritis

The treatment of recognised carditis is unsatisfactory Absolute rest is essential for sudden slight effort even sitting up in bed may prove fatal during the critical period Patients should be nursed flat with one pillow and should have everything done for them including being fed and washed

Diet should be light and fluids limited to two pints daily If there is congestive failure the sodium intake should not exceed 0 5 G daily

Digitalis is dangerous and should only be used in rare cases when atrial fibrillation with a rapid ventricular rate is associated with severe congestive heart failure Quinidine is also dangerous in view of its depressive effect on conduction

THE HEART IN OTHER INFECTIONS

Up to the beginning of the twentieth century it was generally believed that toxic carditis was a common complication of certain fevers such as influenza It came to be recognised however that although cloudy swelling and 'fatty degeneration were often found at autopsy in cases dying from severe general infections clinical evidence of cardiac involvement was rare The change of view followed the establishment of stricter criteria for diagnosing organic heart disease palpitations and irregularities of the heart were shown to be due to autonomic disturbance or to innocent ectopic beats systolic murmurs lost their previous significance, effort syndrome following infections was proved attributable to anxiety X rays failed to confirm clinical cardiac enlargement (based on the position of the apex beat) standard lead electrocardiograms were rarely abnormal The weight of negative evidence was considerable and it became the custom to recognise no form of carditis other than that due to rheumatism or diphtheria In recent years however the earlier view has gained some support particularly owing to the work of Gore and Saphir (1947) who found that diphtheria and rheumatism accounted for less than 25 per cent of fatal cases of myocarditis they contended that carditis was common in a host of infectious diseases including especially scrub typhus bacterial endocarditis and meningococcal septicæmia It may be as well therefore to review the known facts critically for there is grave danger that this modern swing back may go too far

FAILURE OF THE PERIPHERAL CIRCULATION

Cardiovascular disturbances in acute infections are commonly of two kinds and neither is due to a cardiac fault The first is peripheral circulatory failure This may be due to depression of the vasomotor centre to toxic paresis of the vessels themselves to suprarenal failure or to diminution of the blood volume from dehydration or from loss of plasma into the tissue spaces through damaged vessels The essential mechanism is critical discrepancy between the effective vascular capacity and the blood volume so that the central venous pressure falls the cardiac output is reduced and the blood pressure low as in shock

A good sign of vascular relaxation is a markedly dicrotic pulse and although not necessarily serious should put the physician on guard Another significant feature is pallor and coldness of the extremities due to vasoconstriction in the skin this appears to be a compensatory mechanism helping to maintain the venous pressure and blood pressure when dangerous vasodilatation occurs elsewhere e g in muscle Impending failure

of compensatory vasoconstriction may be indicated by waxing and waning of the systolic blood pressure through a range of 10 to 20 mm Hg A fourth indication of circulatory failure is mental confusion or faintness in the sitting posture Whilst tachycardia is the rule and the half hourly pulse chart of some value it should be understood that deceleration sometimes accompanies a falling blood pressure and that the character of the pulse is as important as its rate

Circulatory failure should be treated by nursing the patient flat or with the foot of the bed raised and by the intravenous administration of serum or plasma by the drip method with or without noradrenalin in doses of about 10 μg per minute

The second common cardiovascular reaction to acute fevers is vasomotor neurosis during convalescence This is discussed in Chapter XXII

TOXIC MYOCARDITIS

True toxic myocarditis does occur however especially perhaps in pneumonia Sections reveal focal hyaline necrosis i e granular degeneration and loss of striation of the muscle fibres patchily distributed Cellular reaction with monocytes predominating and fibroblastic repair follow—as in diphtheritic carditis which it resembles This histological picture is common to most forms of carditis—hence the difficulty in making an etiological diagnosis from autopsy findings For example 35 cases of sudden death following tonsillitis or common cold were reported by Gore and Saphir (1947) and ascribed to toxic myocarditis Thirty one of them however could have been due to diphtheria or pneumonia a negative throat swab does not exclude diphtheria

Myocarditis and diffuse glomerulonephritis have long been known to complicate bacterial endocarditis but when the death rate of the septicæmic stage was 98 per cent they received scant attention Since the introduction of penicillin however heart failure from myocarditis has been said to be chiefly responsible for the present 25 per cent mortality nevertheless heart failure is rare in the absence of severe aortic or mitral incompetence and the rapidly progressive mechanical fault could well be to blame

Histological examination of the heart in cases dying from meningococcal infection may disclose evidence of carditis but clinical signs of cardiac involvement are most unusual and the total mortality rate in adults is less than 1 per cent (Daniels *et al* 1943)

Pneumococcal and *streptococcal* myocarditis accompanying pneumonia and scarlet fever respectively are perhaps the most convincing forms of non diphtheritic bacterial toxic myocarditis especially the former Streptococcal myocarditis of this kind bears no resemblance to rheumatic carditis which is a more likely complication of scarlet fever

Tuberculous myocarditis sometimes accompanied by erythema nodosum has been reported in association with primary tuberculosis (Neidhart and Rumrich 1950) but is believed to be allergic in type Six out of 30 cases

of otherwise idiopathic myocardial fibrosis described by Perrin Froment and Lenegre (1953) had pulmonary or mediastinal tuberculosis

Collapse in *typhoid fever* is usually due to peripheral circulatory failure evidence of true myocarditis being unconvincing (Porter and Bloom, 1935) Electrocardiographic changes during the course of typhoid have been reversed within 48 hours of giving 300–600 mg of niacin (nicotinic acid) daily by mouth (Rachmilewitz and Braun 1948) suggesting deficiency of at least one of the B group of vitamins

Carditis accompanying scrub typhus (Tsutsugamushi fever) is clinically unconvincing Although histology may reveal myocardial damage and cellular infiltration in fatal cases (Corbett, 1943) the clinical course of the disease seems to be little influenced by them (Williams *et al* 1944 Berry *et al* 1945) In a series of 184 cases seen within one to four weeks after the acute symptoms had subsided and 10 cases seen during the stage of fever the electrocardiogram was virtually normal (Howell 1945) For further information the reader is referred to the issue of the *American Journal of Hygiene*, May 1945 which is devoted to studies on scrub typhus

Certain *virus infections* are known to cause myocarditis occasionally these certainly include infective mononucleosis mumps and poliomyelitis Saphir (1949) gives a much longer list and includes infective hepatitis and virus pneumonia In the war however I encountered no clinical example of myocarditis associated with infective hepatitis or virus pneumonia despite having well over a thousand cases of the former and nearly 300 of the latter under my care This discrepancy between clinical and pathological data permeates the whole subject In poliomyelitis for example Ludden and Edwards (1949) found microscopic evidence of myocarditis in 14 out of 35 fatal cases whereas Spain *et al* (1950) reported only one instance of clinical myocarditis in 140 cases although typical microscopic changes were found in 12 out of 14 that were fatal I have however seen unquestionable examples of clinical myocarditis in adults associated with glandular fever and mumps

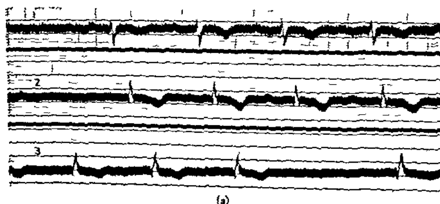
The common cold influenza and other upper respiratory tract infections have been held responsible for many cases of alleged myocarditis but the rarity of any such complication is much more impressive considering the frequency of these maladies in a widespread epidemic of influenza in which clinical evidence of myocarditis was carefully sought, no single example could be found (Wood 1941)

To assess the clinical value of the work of Gore and Saphir quoted above it is worth noting that 16 per cent of their 1 402 cases of myocarditis were due to scrub typhus and there was no evidence that myocarditis was the cause of death Their cases were highly selected excluded children and were based entirely on autopsy findings there were 227 examples of scrub typhus 208 of bacterial endocarditis 144 of diphtheria 130 of rheumatic carditis and 105 of sulphonamide allergy The reader will draw his own conclusions

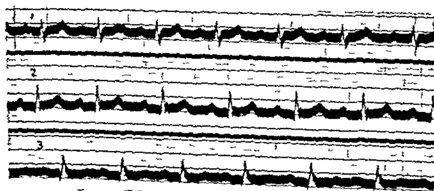
Clinically significant carditis accompanying acute infections in Great Britain (other than rheumatic fever diphtheria and bacterial endocarditis) is undoubtedly rare

Clinical features of toxic myocarditis In acute cases the signs and symptoms are similar to those of diphtheritic myocarditis, except that they may occur earlier during the febrile stage of the infection Symptoms attributable to cardiac involvement may be absent on the other hand there may be dyspnœa unexpected vomiting pallor and peripheral cyanosis due to congestive failure substernal oppression or discomfort or palpitations associated with changes of rhythm It may be difficult to distinguish cardiac symptoms from those due to general toxæmia particularly when there is peripheral circulatory failure Sudden death is not infrequently the first tragic proof of myocarditis

Physical signs include a small rapid thready pulse low systolic blood pressure small pulse pressure gallop rhythm dilatation of the heart,



(a)



(b)

Fig 11 01—Electrocardiogram in a case of toxic myocarditis due to pneumonia
(a) Shows partial heart block with dropped beats and inversion of the T wave in all leads
(b) After recovery

congestive heart failure abnormalities of rhythm and electrocardiographic changes The small rapid pulse and the low blood pressure may equally well be due to peripheral circulatory failure and the gallop rhythm to fever (especially when there is anæmia) The size of the heart may be difficult to assess under the clinical circumstances and the patient should not be moved to the X ray department for more exact information The importance of recognising early signs of congestive heart failure will thus be appreciated Abnormalities of rhythm are also important and include all grades of heart block auricular flutter or fibrillation and paroxysmal tachycardia The electrocardiogram is especially helpful not only in establishing the nature of a rhythm change but also in revealing partial heart block and abnormalities of the T wave (fig 11 01)

Sometimes the course of toxic myocarditis is subacute or chronic The clinical features then closely resemble those of isolated myocarditis (q v)

Prognosis If the diagnosis is beyond doubt the outlook is grave, the mortality rate probably approaching 50 per cent Whether central or peripheral in mechanism the combination of hypotension and a small rapid pulse is always dangerous and congestive heart failure often proves fatal Abnormalities of rhythm and alterations of the T wave without the manifestations just mentioned are less serious

Many cases of mild toxic myocarditis must pass unrecognised but this is not a matter for concern for recovery appears to be complete in all non fatal cases

Treatment Bed rest and specific chemotherapy (when applicable) for all acute infections are axiomatic bed rest should be absolute if the cardiovascular system is involved The patient should be nursed in the position of maximum comfort but if the blood pressure is below 100 mm Hg and there is no evidence of congestive failure he should be kept horizontal if there is congestive failure he should be propped up at 30 to 45 degrees against a back rest Digitalis should be avoided unless there is frank congestive failure for it increases the risk of sudden death from ventricular fibrillation and may aggravate minor degrees of heart block If the venous pressure is well raised and the liver distended however it should not be withheld and it may be invaluable in ca es of auricular flutter or fibrillation Mersalyl and a low sodium diet may be given if there is fluid retention Quinidine or procaine amide may have to be used in cases of paroxysmal ventricular tachycardia but its depressive effect on conduction can be very dangerous if there is already partial heart block

It must be admitted however that toxic myocarditis is little influenced by therapy and is apt to be fatal or otherwise according to its severity

MYOCARDITIS DUE TO PARASITES

A most convincing form of protozoal myocarditis may accompany *South American trypanosomiasis* or Chagas disease (Chagas 1909) Leish

manial forms of *T cruzi* multiply chiefly in the cells of the heart brain and liver the affected cells finally rupture and liberate the parasites into the blood stream An intense local inflammatory reaction follows The signs and symptoms of a typical acute or subacute myocarditis may dominate the clinical picture and sudden death is common (Mosely and Miller 1945) The clinical diagnosis may be suggested by associated encephalitis and may be proved by demonstrating the parasites in the blood stream

Of the protean manifestations of *toxoplasmosis* myocarditis must be relatively rare but three cases have been reported recently by Paulley *et al* (1954) and others may come to light now that serological tests are likely to be performed in cases of myocarditis of uncertain etiology The protozoal intracellular parasite known as toxoplasma seems to be far more widespread in man than originally suspected but the majority of individuals with positive serological tests give no indication of disease The best known clinical reactions are cerebral and ophthalmic whether congenital or acquired (Vail *et al* 1943 Ridley 1949) If there is a myocardial reaction however a clinical picture resembling that of isolated myocarditis may arise or myocarditis may complicate more familiar manifestations of the disease The diagnosis is strongly supported by a specific complement fixation test at titres of 1/16 or higher

Trichiniasis is rarely complicated by myocarditis, and even minor electrocardiographic abnormalities are uncommon Thus of 44 cases investigated by Beecher and Amidon (1938) only one had a slightly prolonged P R interval and one sino auricular block Solarz (1947) found transient flat or inverted T waves in 16 out of 114 cases (14 per cent) but no clinical evidence of myocarditis in any of them Allergic reactions to trichiniasis occur however and rare instances of myocarditis may perhaps be of this kind

Schistosomiasis is more likely to affect the heart by causing pulmonary hypertension from obliterative pulmonary endarteritis than myocarditis although I have seen a pathological specimen of the latter in South Africa Cor pulmonale due to bilharzia is described in chapter XVIII

There is little evidence that *malaria* causes myocarditis collapse is usually due to peripheral circulatory failure

A *hydatid cyst* may be found in the heart or pericardium as a result of a routine skiagram of the chest but is rarely recognised clinically unless it ruptures This is a space filling lesion rather than a myocarditis The electrocardiogram may show reduced R waves and inverted T waves in chest leads taken from points overlying the cyst Rupture may be into the pericardial sac or into any of the cardiac chambers (Canabal *et al* 1955) The differential diagnosis is from other pericardial cysts cardiac tumours mediastinal cysts and neoplasms and cardiac aneurysm Echinococcal cysts elsewhere the Casoni test and the complexion fixation test help to establish the diagnosis

MYOCARDITIS DUE TO FUNGI AND YEASTS

Actinomycosis involves the heart in less than 2 per cent of cases (Kasper and Pinner, 1930) When it does so the fungus usually reaches the heart by direct extension from infected neighbouring structures, so that pericarditis occurs first, but initial myocarditis from hæmatogenous spread has also been reported (Cornell and Shookhoff 1944) Clinically, the majority of cases have been recognised owing to the development of congestive heart failure, signs of pericarditis have been detected less frequently Treatment includes heavy and prolonged doses of sulphonamides penicillin and surgery (Lyons *et al* 1943 Zoeckler 1951)

Myocardial *coccidioido mycosis* was found in 11 out of 48 cases included in the series reported by Gore and Saphir (1947) Clinically, however myocardial involvement is rare Thus in a large epidemic of 75 cases described by Goldstein and Louie (1943), all but one recovered without evidence of carditis In this group the incubation period was 14 days Symptoms and signs included fever pleurisy cough with brownish or blood stained sputum, cervical adenitis erythema nodosum or multiforme and bilateral hilar opacities extending outwards into the central zone of the lungs Leucocytosis, eosinophilia and a high sedimentation rate were the rul The diagnosis can be confirmed by a specific skin sensitivity test a complement fixation test and by identifying the fungus in the sputum

Histoplasmosis is sometimes mentioned as a cause of myocarditis by yeast like organisms, but in a review of 71 cases Parsons and Zarafonetis (1945) found little evidence to support this statement There were four instances of vegetative endocarditis, two of them involving the tricuspid valve but no convincing examples of frank myocarditis

ISOLATED MYOCARDITIS

Isolated myocarditis (Scott and Saphir, 1929) is a subacute or chronic inflammation of the heart of unknown etiology characterised by patchy myocardial necrosis cellular infiltration and fibroblastic repair, as in other forms of myocarditis It was first properly described by Fiedler (1899) The disease may not be a specific entity and is difficult to distinguish pathologically from known forms of toxic or infective myocarditis of relatively long duration

Incidence Although still relatively rare isolated myocarditis is being recognised with increasing frequency The majority of cases have occurred in subjects between the ages of 20 and 50 but infants children and old people are not exempt The disease has been reported sporadically in most countries and races and accounts for about half of all cases that present clinically with heart failure of unknown etiology

Pathology Patchy necrosis of muscle is thought to be the primary lesion (fig 11 02) Cellular reaction may be focal or more diffusely interstitial



(a)



(b)

Fig 11 02—Focal necro is in a case of Fiedler s carditis
(a) Low power
(b) High power The cells are macrophages plasma cells lymphocytes and eosinophils
(By ourt sy f Pr f C I Harr so)

Monocytes predominate but in the acute stage polymorphs may be more numerous Hæmorrhage and exudate may occur Giant cells eosinophils and arteritis suggest another etiology—allergy Fibroblastic repair follows As a rule all stages of activity and healing are seen in the same specimen occasionally, extensive interstitial fibrosis is found alone and is believed to represents the end result of the same process As a rule these hearts weigh 500–600 G and are usually very dilated

The pericardium, endocardium and valves are not involved, but mural thrombi are common and may give rise to emboli and infarcts in other organs (Scott and Saphir 1929 Davies *et al* 1951)

Clinical features The history is invariably short, rarely longer than a few months The chief symptoms are increasing dyspnœa and fatigue, sometimes there is atypical angina pectoris or substernal discomfort (Hansmann and Schenken 1938) or an attack of pain may be so severe and prolonged as to suggest cardiac infarction (Gillis and Walters 1954) occasionally hemiplegia or hæmoptysis signals the onset (Josserand and Gallavardin 1901 de la Chapelle and Graef 1931)

The physical signs are usually those of congestive heart failure with a normal or low blood pressure small pulse pressure sinus tachycardia peripheral cyanosis and pallor cold extremities general enlargement of the heart (fig 11 03) gallop rhythm and normal valves Disturbances of rhythm particularly paroxysmal tachycardia atrial flutter and partial heart block are not uncommon

The *electrocardiogram* often shows left bundle branch block Not infrequently rather low voltage and simple inversion of the T waves in most leads may suggest Pick s disease Occasionally a relatively large zone of necrosis in the wall of the left ventricle may give rise to pathological Q waves and inverted T waves resembling the pattern of cardiac infarction In one case Bayley (1946) recorded typical anoxic depression of the RS T segment and attributed it to the fact that the lesions were mainly close to the endocardium of both ventricles

Radiographic appearances include moderate or considerable enlargement of the heart shadow particularly the left ventricle varying degrees of pulmonary venous congestion and dilatation of the right atrium and superior vena cava the aorta pulmonary artery and left atrium usually look normal

There is no fever, no leucocytosis no eosinophilia and no rise of sedimentation rate No special diagnostic tests are available

Differential diagnosis The case usually presents as one of heart failure of uncertain etiology It is at once distinguished from the *hyperkinetic circulatory states* (e g anæmia beri beri arteriovenous aneurysm Paget s disease of bone thyrotoxicosis anoxic pulmonary heart disease uræmia and certain diseases of the liver) by the obviously low cardiac output and signs of peripheral vasoconstriction

In middle aged or elderly subjects *ischæmic heart disease* may be difficult



Fig 11 03—Skiagram showing general enlargement of the heart in a case of Fiedler's myocarditis

to exclude if there is a history of angina pectoris or electrocardiographic evidence suggesting active ischæmia or an actual infarct In these unusual cases however, there is apt to be some discrepancy between the clinical situation and the suggested diagnosis of coronary disease for example there may be advanced congestive failure with minimal ischæmic changes in the electrocardiogram persistent heart failure may ante date pain the QT pattern suggesting infarction is rarely well developed and the S T segment is never conspicuously elevated A normal blood cholesterol and normal lipo proteins should add to the doubt

Hypertensive heart disease in which the blood pressure has temporarily fallen is seen occasionally but such a diagnosis should never be accepted readily without historical or subsequent proof (Kaplan Clark and de la Chapelle 1938)

Aortic stenosis with a minimal murmur heard best at the apex beat may be mistaken for isolated myocarditis with left ventricular failure and functional mitral incompetence The quality of the peripheral pulse an aortic ejection click the timing of the aortic murmur reversed splitting of the second heart sound (in the absence of left bundle branch block), and careful screening for calcium in the aortic valve should prevent error

Pericardial effusion may be closely simulated The apex beat however is usually more forceful in isolated myocarditis and much displaced to the left pronounced gallop rhythm points to a myocardial fault as does left bundle branch block Diagnostic paracentesis or cardiac catheterisation settles any lingering doubts

Chronic constrictive pericarditis without calcification can be clinically impossible to distinguish from isolated myocarditis, as emphasised by Davies *et al* (1951) A paradoxical pulse impalpable cardiac impulse and absence of gallop rhythm are all in favour of Pick s disease whilst a strong cardiac impulse functional tricuspid incompetence and left bundle branch block are all in favour of myocarditis but a small peripheral pulse high venous pressure steep *y* descent conspicuous *y* trough positive or negative Kussmaul sign absence of murmurs gallop rhythm T wave inversion maximal in leads V_5 and V_6 and moderate general enlargement of the heart shadow all occur frequently in both conditions *Routine cardiac catheterisation* does not distinguish them for in both the cardiac output is low left and right atrial pressures are high and more or less equal steep *y* descents followed by conspicuous *y* troughs and ventricular overshoots are seen on both sides of the heart and the pulmonary vascular resistance is normal (fig 11 04) Special physiological tests for distinguishing the two are under trial but have so far proved unreliable for cases of Pick s disease sometimes behave physiologically like cases of heart failure it is doubtful however if cases of heart failure ever behave like cases of uncomplicated Pick s disease The tests include direct measurement of change in cardiac output brought about by alterations in right ventricular filling pressure the

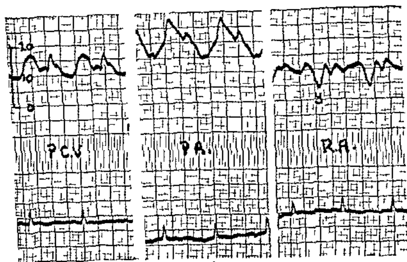


Fig 11 04—Pressure pulses from a case of isolated myocarditis showing high atrial pressures and a conspicuous *y* trough in the right atrial tracing

effect of Valsalva s manœuvre on the brachial arteriogram and the effect of change of posture on the digital pulse (see pages 292 and 293)

A *primary change of rhythm* particularly paroxysmal ventricular tachycardia in young persons or paroxysmal atrial flutter or fibrillation in later life may cause considerable diagnostic difficulty when attacks are prolonged recurrent and difficult to control for severe heart failure may well occur under such circumstances and if the patient is examined during a short period of normal rhythm there is likely to be a raised venous pressure gallop rhythm low blood pressure small pulse considerable cardiac enlargement and widespread inversion of the T waves in the electrocardiogram, it is easy then to assume that the rhythm change was secondary to myocarditis The life and future good health of the patient may well depend on a more enlightened view which is that every case of heart failure of uncertain etiology associated with an important change of rhythm should be regarded as secondary to that rhythm change until proved otherwise Every effort must be made to restore normal rhythm and to maintain it for at least six weeks, by the end of that time nutritional changes in the myocardium should have cleared up completely if the change of rhythm was primary

Once it has been concluded that the case is one of isolated myocarditis or one of the many other cardiopathies described in this chapter a serious attempt should be made to identify its nature This may involve much time and labour and the results are usually negative and disheartening but any other attitude must halt progress in this baffling field

Course and prognosis All proven cases have naturally been fatal even so, there have been no reports of probable cases that have survived Death

has usually occurred within a few weeks to a year or two of making the diagnosis or of admitting the patient to hospital

Treatment Absolute rest in bed digitalis, mercurial diuretics and a low sodium diet may help but the general response is poor Neither cortisone nor A C T H has proved of any value even in large doses

ENDOMYOCARDIAL FIBROSIS

In recent years considerable interest has been aroused by an obscure cardiopathy characterised by extensive endocardial and subendocardial fibrosis When the endocardium is thick and white it resembles congenital fibroelastosis when the fibrosis is chiefly subendocardial the pathology is more like the most chronic form of isolated myocarditis or the most fibrotic form of nutritional cardiopathy described later It is therefore difficult to classify and until its etiology is understood it may be best to regard it as a special form of isolated myocarditis this at least emphasises our ignorance concerning its nature

The 40 cases in African troops serving in the Middle East described by Bedford and Konstam (1946) were having an adequate diet far better than they were accustomed to at home There were 17 necropsies in this series and the fibrosis was mainly subendocardial the authors thought the pathology resembled that of isolated myocarditis more closely than any other disease Davies (1948) described a very similar disease in 36 East African natives (32 male) at autopsy the heart was dilated rather than hypertrophied as in the series just quoted but the fibrosis involved the endocardium as well as the subendocardial myocardium The left ventricle was again chiefly involved and there was the same frequency of mural thrombosis as has been noted in nearly all forms of heart failure of obscure origin whether inflammatory allergic or nutritional A third series of 25 cases similar to Davies was reported by O Brien (1954) in the Sudan The diet was normal in 23 of them and alcoholism could be excluded The patients were older than the others averaging 54 years Functional mitral and tricuspid incompetence was stressed but it is doubted whether this had any special significance

Becker Chatgidakis and Van Lingen (1953) claimed that endomyocardial fibrosis was a diffuse collagen disease There were 32 Bantu subjects amongst their 40 cases but they did not blame the diet They also stressed cardiac dilatation rather than hypertrophy and the frequency of mural thrombosis The earliest lesion demonstrable was focal endocardial mucinous œdema similar lesions occurred as eccentric foci in the sub intimal tissues of the small blood vessels of the myocardium In addition interstitial myocardial œdema, attributed to increased capillary per meability, caused muscle bundles to be widely separated Fibrinous exuda tion was closely related to the areas of mucinous œdema and was the fore runner of mural thrombosis Foci of fibrinoid necrosis were seen in

well established areas of mucinous œdema In subacute cases cellular infiltration and granulomatous tissue appeared in the affected zones In chronic cases progressive fibrosis resulted in endocardial sclerosis myocardial fibrosis and eccentric subintimal connective tissue cushions' The authors thesis was that the general design of the changes described was characteristic of all collagen diseases

Clinically cases of endomyocardial fibrosis usually present as examples of heart failure of uncertain etiology Failure may be chiefly left sided or congestive Details are identical with those of isolated myocarditis

COLLAGEN DISEASES AND ALLERGIC STATES

These include rheumatoid arthritis periarteritis nodosa disseminated lupus scleroderma dermatomyositis and Loffler s syndrome In all these conditions the clinical features of the cardiopathy closely resemble those of isolated myocarditis and will not therefore be discussed in detail again but each has specific features by which it may often be identified at the bedside or in the laboratory and these must be briefly described

Rheumatoid arthritis

Rheumatoid itself is too familiar to warrant detailed description here but it should be borne in mind that joint manifestations superficially resembling rheumatoid may occur in any of the collagen diseases particularly scleroderma

The heart may be involved in cases of rheumatoid in three different ways (1) chronic valve lesions indistinguishable from and probably identical with those following rheumatic fever are found in about 10 per cent (2) clinical pericarditis is not uncommon and necropsy evidence of healed pericarditis is found in 40 per cent of cases (3) a specific focal granulomatous myocarditis has been described by many authors in 1 to 3 per cent of cases (Sokoloff 1953) In addition severe secondary anæmia may affect the cardiovascular system

In differential diagnosis the following general rules may be found helpful in practice

1 Acute or subacute endocarditis in children with Still s disease and chronic valve lesions in adults with frank rheumatoid arthritis should be attributed to coincident or past rheumatic carditis respectively
2 Isolated pericarditis in children with Still s disease or in adults with rheumatoid may be attributed to the rheumatoid state with reasonable confidence but not to the neglect of excluding tuberculosis
3 A patient presenting with the combination of clinical rheumatoid arthritis and a cardiopathy resembling isolated myocarditis is more likely to have scleroderma or one of the other collagen diseases than true rheumatoid even cor pulmonale with secondary osteo arthropathy is more likely

Periarteritis

Periarteritis nodosa or polyarteritis is a manifestation of hypersensitivity (Rich 1942 Rich and Gregory, 1943) and may be provoked by a variety of antigens (Miller and Daley 1946) It is characterised by disseminated or patchily distributed segmental arteritis the initial lesion being fibrinoid necrosis of the media and internal elastic lamina cellular infiltration and secondary thickening of the intima Small aneurysms develop in about *16 per cent of cases* (*Harris Lynch and O Hara 1939*) Serious disturbances of function occur in the systems chiefly affected

The disease may occur at any age but particularly in young adults and is three times as frequent in males as in females

Cases tend to sort themselves into well defined patterns according to the system or combination of systems chiefly involved These patterns include pyrexia of uncertain origin, peripheral neuritis (Kernohan and Woltman 1938) nephritis (Davson Bell and Platt 1948) hypertension bronchial asthma (Harkavy, 1941), obscure abdominal pain (Harris Lynch and O Hara 1939) and myocarditis It is only the last of these with which we are here concerned but when an obscure cardiopathy is accompanied by any of the other manifestations mentioned periarteritis should be seriously considered

Confirmatory evidence includes almost any form of allergic rash visible or palpable nodules along the course of a superficial artery such as the temporal changes in the ocular fundus (including exudates hæmorrhages papillœdema retinal detachment vascular irregularities and occlusion of the central artery of the retina (Sampson 1945)) leucocytosis eosinophilia rapid blood sedimentation rate positive C reactive protein test and above all a positive muscle or liver biopsy

Loffler s syndrome

Loffler (1932 1936) described a subacute condition of the lungs characterised by transitory infiltrative lesions and eosinophilia This seems to be similar to pulmonary periarteritis as described by Elkeles and Glynn (1944)

Allergic myocarditis

Eosinophilic myocarditis as described by Reinhart (1946) and others is also likely to be a variant of polyarteritis

Sulphonamides have been accused of acting as antigens that may provoke allergic myocarditis (French and Weller 1942 French 1946) but a careful control study by Fawcett (1948) does not support this hypothesis

Disseminated lupus

Disseminated lupus is regarded as a widespread necrosis of connective tissue particularly fibrinoid degeneration of collagen fibres (Klemperer

Pollack and Baehr 1941) resulting from some crucial disturbance of antigen antibody reaction

Like periarteritis it affects chiefly young adults but unlike periarteritis it attacks women in 90 per cent of cases A previous history of lupus erythematosis (butterfly rash) is obtained in at least one third of all cases The illness is apt to be precipitated by some infection drug therapy or physical agent (such as sunburn)

The clinical features include fever patchy erythematous rashes painless erythematous macules (usually in the thenar or hypothenar emminences) tender nodules more deeply situated in the skin (like Osler s nodes) hyperæmia of the nail folds petechiæ or purpura small hæmorrhagic necrotic lesions in the fingers or mouth polyarthritis not unlike that seen in rheumatic fever generalised adenopathy transient infiltrative lesions in the lungs which may cause hæmoptysis vascular lesions in the ocular fundus and cardiac manifestations consisting of pericarditis myocarditis and the verrucous endocarditis of Libman and Sachs (1924) Pericardial effusion may occur (Humphreys 1948) The myocarditis itself behaves functionally like isolated myocarditis Endocarditis when present is apt to affect the tricuspid as well as the mitral or aortic valve The vegetations are larger than in rheumatic valvitis but less damaging than in bacterial endocarditis Histological details have been given by Gross (1940) and the subject has been well reviewed by Griffith and Vural (1951)

The diagnosis of disseminated lupus may be confirmed by leucopenia thrombocytopenia hypochromic anæmia a raised sedimentation rate absence of C reactive protein the presence of cold agglutinins L E cells in the bone marrow and peripheral blood hyperglobulinæmia increased gamma globulin reversal of the albumin/globulin ratio and increased heparin tolerance These tests have been reviewed by Gold and Gowing (1953)

Scleroderma

Another collagen disease that may affect the heart is scleroderma Here the connective tissue of the skin, œsophagus joints and heart is chiefly and diffusely involved

The sexes are about equally affected and the average age is nearer 40 than 30

In addition to the smooth shiny fixed skin of the affected areas the majority of cases have Raynaud s syndrome (often the first symptom) polyarthritis (like rheumatoid) and pigmentation of the exposed surfaces of the skin (Weis *et al* 1943) About half the cases have some difficulty in swallowing and reduced peristalsis with delay in the passage of barium through the œsophagus may be demonstrated radiologically (Olsen *et al* 1945) Occasionally the lungs are involved and rarely the kidneys

Many cases of scleroderma heart disease have been reported the majority

proving fatal within a year or two There is an increase of cellular vascular connective tissue with secondary degeneration of muscle fibres followed by replacement fibrosis

There are no specific laboratory tests for scleroderma except the microscopic appearances of biopsied skin Patients are usually afebrile but may have a raised sedimentation rate The C reactive protein test is negative but the serum globulin may be increased For diagnostic purposes clinical hall marks are more helpful

Dermatomyositis is similar to scleroderma in most of the above respects but involves muscle as well as skin (Tager and Grossman, 1944)

Treatment of myocarditis due to collagen diseases

Few cases of myocarditis due to any of the collagen diseases or allergic states (except rheumatic carditis) survive more than two years whatever treatment is given A C T H, cortisone, hydrocortisone or preferably one of the newer compounds such as decortisyl (delta 1 dehydrocortisone) that do not cause sodium retention may be tried The usual dose of cortisone in these cases is 200–300 mg daily for the first week 100–150 mg daily for the second, and 50–75 mg daily for the third it is then gradually reduced to the minimum that seems to control the disease A strict low sodium diet and mercurial diuretics help to combat sodium retention The dose of decortisyl is one quarter of the dose of cortisone Withholding the drug all too frequently results in a violent exacerbation of activity and few cases derive much benefit Disseminated lupus responds best (Cohen and Cadman 1953)

Sarcoidosis

The precise nature of sarcoidosis is still uncertain (Scadding 1950) It may affect the cardiovascular system in two ways, both of which are rare extensive pulmonary involvement may cause cor pulmonale (q v) or there may be an actual sarcoid myocarditis

The clinical features of the cardiopathy resemble those of isolated myocarditis cases may present with congestive failure (Yesner and Silver 1951) or with cardiac pain, suggesting ischæmic heart disease (Stephen 1954), sudden death may occur

The diagnosis may be suggested by coincident pulmonary lesions mediastinal or generalised lymphadenopathy splenomegaly erythema nodosum iridocyclitis and hyperglobulinæmia it may be confirmed by biopsy of an enlarged gland, skin lesion or liver In doubtful cases a saline emulsion of sarcoid tissue may be injected intradermally (Kveim test) the insidious development of a dusky red nodule at the site of injection having the histological appearances of sarcoid is diagnostic (James and Thompson 1955)

METABOLIC AND NUTRITIONAL CARDIOPATHIES

These include primary amyloidosis hæmochromatosis diabetes mellitus beri beri alcoholism and perhaps endomyocardial fibrosis a congenital group comprising fibroelastosis anomalous origin of the left coronary artery from the pulmonary artery Von Gierke s disease gargoylism and possibly familial cardiomegaly, has already been described in Chapter VIII and is therefore omitted here

Primary amyloidosis

This is a rare metabolic disorder of unknown etiology affecting middle aged or elderly persons of either sex The heart is involved in 85 per cent of cases (Eisen 1946) seriously so in at least 50 per cent (Lindsay 1946) Amyloid material accumulates in the interstitial spaces between secondarily atrophic muscle fibres, and in the walls of the blood vessels (Larsen 1930)

The majority of cases present clinically like isolated myocarditis i e with congestive heart failure of obscure etiology There are very few clues pointing to the true nature of the cardiopathy—only the age of the patient which is usually over 50 (Jones and Frazier 1950) macroglossia and profound asthenia (Eisen 1946) There is of course no history of chronic suppuration or other infection in these primary cases and the congo red test is negative Virtually all laboratory tests selected in the hope of identifying the nature of an obscure cardiopathy are negative except biopsies of the tongue, or possibly skeletal muscle which may reveal amyloid

The two most important diagnostic errors are (1) mistaking amyloid for Pick s disease which may lead to a fruitless and dangerous thoracotomy (Couter and Reichert 1950) and (2) misinterpreting abnormal Q or QS waves and inverted T waves in the electrocardiogram as evidence of cardiac infarction (Wessler and Freedberg 1948 Holzmann 1950) The differential diagnosis between both these conditions and isolated myocarditis has already been discussed

Hæmochromatosis

The disorder of iron metabolism known as hæmochromatosis may affect the heart as well as the pancreas liver, testicles adrenals skin and other organs Althausen and Kerr (1933) emphasised the serious consequences of cardiac involvement and in his classic monograph Sheldon (1935) stated that heart failure was the cause of death in 15 per cent of 119 cases Iron is absorbed avidly from the intestinal tract reaches a relatively high level in the blood is poorly excreted and is deposited in the organs mentioned above Diabetes mellitus muddy pigmentation of the skin loss of axillary and pubic hair testicular atrophy and impotence cirrhosis of the liver and heart failure are the chief consequences Deposition of iron in the muscle fibres of the heart is common in cases without disturbance of

cardiac function (de Gennes *et al*, 1936), but it has usually been more conspicuous in cases of heart failure and secondary fibrosis more evident

Of the 311 cases reviewed by Sheldon (1935) about 95 per cent were men The usual age is between 45 and 60 but cardiac cases tend to be younger all but three out of 25 such cases reviewed by Petit (1945) being under 45

The chief cardiac manifestations are disturbances of rhythm (including heart block and ventricular fibrillation) and heart failure which may be mainly left ventricular or congestive' but pain resembling that in ischæmic heart disease may occur (Horns, 1949) as in isolated myocarditis

The diagnosis is usually obvious owing to the many characteristic features of the disease as a whole, but when the heart bears the brunt of the attack in a young adult it may be overlooked Hæmochromatosis may be proved by biopsy of the skin or liver (King and Downie, 1948) Absorption storage and excretion of iron may be studied by giving radioiron and following its course in the fæces blood and body organs (Bothwell *et al* 1952)

Diabetes mellitus

The relationship between diabetes, blood lipids atherosclerosis peripheral vascular disease and coronary disease is familiar if not fully understood In addition some confusion may be caused by the presence of depressed S T segments or inverted T waves in the electrocardiogram in patients without other evidence of coronary disease these appearances have been attributed to a low blood potassium following treatment for diabetic acidosis (Liebow and Hellerstein 1949 Henderson 1953) too much insulin therapy may also precipitate or aggravate latent angina pectoris for hypoglycæmia causes hyperadrenalism and this too may alter the electrocardiogram Finally, circulatory collapse in diabetic coma may temporarily impair the nutrition of the myocardium Apart from these considerations diabetes mellitus does not injure the heart

The heart in malnutrition and chronic alcoholism

The heart may be seriously affected by nutritional anæmia and beri beri, both conditions give rise to a hyperkinetic circulatory state and are discussed under that heading The term *nutritional cardiopathy* is best reserved for that form of heart disease that may result from an unbalanced high carbohydrate low protein diet as described by Gillanders (1951). The disorder is common amongst the adult Bantu population of South Africa and something very similar may be seen in chronic alcoholics anywhere At necropsy the heart is dilated and hypertrophied and microscopy shows hypertrophy of the muscle fibres without loss of striation or hydropic degeneration intracellular œdema may occur but is not specific being found in many types of heart failure patchy interstitial fibrosis is also described but may be inconspicuous There are no inflammatory foci and

the endocardium is normal except where it underlies organised mural thrombi which are common in both ventricles and atria In other words the findings are simply those of chronic heart failure without demonstrable cause (Higginson Gillanders and Murray 1952) Varying degrees of cirrhosis of the liver thought to be due to the same malnutrition are found in nearly all cases heavy deposits of hæmosiderin are common in the liver and other abdominal organs but not in the heart itself

The post mortem findings in chronic alcoholics dying from heart failure are similar although the intracellular œdema has been specially emphasised (Merle and Belin 1953) The hepatic hypoproteinæmic metabolic cardiopathy described by Oppenheim (1950) in cases of cirrhosis of the liver may be similar but may also include hepatic hyperkinetic circulatory states

Clinically cases present with the characteristic dietetic or alcoholic history and congestive heart failure with a low cardiac output Atrial flutter is particularly common in alcoholic cases

The *differential diagnosis* is from beri beri hæmochromatosis and hepatic cardiopathy Beri beri is excluded by the low cardiac output absence of response to aneurin and negative biochemical and biological tests for aneurin deficiency Cases may occur however in which B1 deficiency is also present and therapeutically it is wise to cover the possibility Hæmosiderosis may be found in hepatic biopsies and is believed to be another result of chronic malnutrition (Gillman and Gillman 1951) hæmochromatosis involving the heart is unlikely in the absence of any other evidence of that disease Associated cirrhosis of the liver may be advanced especially in chronic alcoholics and may lead to vasodilatation and an attempt to raise the cardiac output The combination of nutritional and hepatic cardiopathies may be confusing and may result in an erroneous diagnosis of beri beri but the hepatic palms spider nævi small volume collapsing pulse low blood pressure and absence of response to thiamine should soon correct the mistake

Treatment consists of a high protein well balanced diet which if given in time may reverse the myocardial fault Too often however it is already too late or the diet is not maintained The usual remedies for heart failure must also be prescribed

ENDOCRINE CARDIOPATHIES

Thyrotoxicosis and myxœdema are by far the most important endocrine diseases that affect the cardiovascular system They are discussed separately in Chapter XIX

Acromegaly may cause considerable cardiac hypertrophy and hyperplasia of interstitial fibrous tissue Enlargement of other viscera usually accompanies the cardiomegaly Many hearts from acromegalics have weighed over 1 000 G (Courville and Mason 1938) Hypertension and coronary disease associated with diabetes complicate some of the cases but

heart failure may occur in their absence (Hejtmancik Bradfield and Herrman, 1951) Failure is attributed to enlargement outstripping nutritional supplies

NEUROMUSCULAR DYSTROPHIES

Friedreich's ataxia has been discussed in the congenital section

Progressive muscular dystrophy involves the heart in about 50 per cent of cases (Rubin and Buchberg 1952) There is muscular atrophy and fibrous tissue replacement (Weisenfeld and Messinger 1952) There seems to be little relationship between the degree and severity of the skeletal myopathy and the cardiac lesion

The great majority of cases are male and the average age 25 (*Zatuch et al* 1951)

Clinically the most common finding is some abnormality in the electrocardiogram such as bundle branch block or T wave changes without serious disturbance of cardiac function Arrhythmias also occur, and in a minority congestive heart failure Sudden death has been reported in several instances

The diagnosis should be suggested by the prominent yet weak calf muscles the awkward gait and the habit of climbing up the legs when getting up it may be proved by muscle biopsy

TUMOURS OF THE HEART

Primary tumours are rare and include myxoma (35 per cent) sarcoma (21 per cent) fibroma (12 per cent) rhabdomyoma (19 per cent) and lipoma (12 per cent) (Yater 1931) Secondary tumours are sixteen times more common (Reeves and Michael, 1936) they have been found at necropsy in 10 per cent of all cases of malignant disease but have given rise to clinical manifestations in only 1 per cent (Goudie 1955) The majority are secondary to carcinoma of the bronchus or breast but almost any malignant tumour may metastasise to the heart (Raven 1948 Young and Goldman 1954) Leukæmia must also be considered in this section

MYXOMA OF THE LEFT ATRIUM is the commonest primary tumour of the heart It arises from the atrial septum to which it is attached by a pedicle close to the foramen ovale

The majority of patients have been women between the ages of 30 and 60

Symptoms may develop relatively suddenly and are attributable to acute subacute chronic or paroxysmal obstruction at the mitral orifice Severe syncopal attacks during which the pulse may be imperceptible acute pulmonary œdema or paroxysmal nocturnal dyspnœa may occur A chronic course ending in congestive heart failure has also been described Arrhythmias are said to be infrequent but paroxysmal atrial tachycardia and atrial fibrillation have both been recorded (Gilchrist and Miller 1936 Fawcett and Ward 1939)

The physical signs include a small peripheral pulse and remarkably variable mitral systolic and diastolic murmurs In some cases however no murmurs are heard at all (Von Reis 1949) The records in the literature rarely mention the first heart sound or the presence or absence of a mitral opening snap but Burnett and Davidson (1945) stated that the first heart sound was accentuated in their case as did Jones and Julian (1955) and all observers have likened the signs to those of variable mitral stenosis with or without pulmonary hypertension (Mahaim 1947) The P wave of the electrocardiogram has usually been more or less normal and as a rule X rays have revealed little enlargement of the left atrium and pulmonary artery Few illustrations of chronic pulmonary interstitial œdema have been published

The physiological findings on cardiac catheterisation may prove as variable as the murmurs and this itself may suggest the correct diagnosis myxoma should also be suspected if the left atrial pressure is found to be normal in a case of supposed mitral stenosis giving a history of paroxysmal cardiac dyspnœa Angiocardiography may reveal a filling defect of the left atrium (Goldberg and Steinberg 1955)

In the case reported by Jones and Julian (1955) the mean left atrial pressure was 44 mm Hg and the mean pulmonary artery pressure 80 mm Hg Left atrial pressures as high as this at rest are very unusual in mitral stenosis particularly in cases with so short a history Even passive pulmonary hypertension of this degree could well cause right ventricular failure

The downhill course is usually rapid few patients surviving more than a year after the onset of symptoms Death may terminate a syncopal attack or result from acute pulmonary œdema

Treatment is surgical In cases of acute pulmonary œdema or loss of consciousness it is worth changing the position of the patient in the hope that the tumour may slip away from the mitral orifice

PRIMARY SARCOMA of the heart arises from the right atrium in at least half the cases (Weir and Jones 1941) and as it grows tends to fill the cavities of both the right atrium and right ventricle Hæmangioendothelio sarcoma behaves similarly (Cheng and Sutton 1955 Amsterdam *et al* 1949) These tumours may be highly vascular and are composed *chiefly* of nests of hæmangioblasts in a groundwork of endothelial cells

The clinical features of sarcoma of the right atrium closely resemble those of rapidly progressive tricuspid stenosis the obstruction of the circulation being more or less at the level of the tricuspid valve through which the tumour usually grows

FIBROMA is most likely to involve the wall of the left ventricle The only example I have seen was in a female child who presented with paroxysmal ventricular tachycardia heart failure which finally proved fatal an electro cardiogram with a QT pattern suggesting cardiac infarction in anterolateral



Fig 11 05—Fibroma of the left ventricle (Ack ldgm tt D U la Jame)

left ventricular surface leads or their equivalents and radiological appearances resembling a large left ventricular aneurysm (fig 11 05)

RHABDOMYOMA is a congenital glycogen containing tumour of heart muscle fibres (ῥαβδος a rod) and is more often multiple than solitary The nodules are usually found in the wall of the left ventricle and may be associated with tuberose sclerosis Most cases die in infancy or childhood (Batchelor and Maun 1945)

SECONDARY TUMOURS involve the heart or pericardium in about 10 per cent of all cases of cancer (Scott and Garvin 1939) The majority are secondary to bronchial carcinoma and invade the heart by direct extension the pericardium being affected first Thymic and other mediastinal neo plasms may spread to the heart in the same way

Clinically such cases tend to present with hæmopericardium often with cardiac tamponade in others paroxysmal atrial tachycardia or flutter is the first manifestation Sometimes pericardial pain and inverted T waves in the electrocardiogram are mistaken for cardiac infarction especially when followed by intractable heart failure

Discrete blood born secondary nodules from remote malignant growths are less frequent and when present may be associated with more obvious secondaries in the lungs

LEUKÆMIA may give rise to infiltrative myocardial or pericardial lesions but they are rarely of much clinical importance Associated severe anæmia is more likely to embarrass the cardiovascular system I have only seen five cases of leukæmia amongst my last 10 000 patients with cardiovascular disease three of these presented with acute cardiac infarction from coronary thrombosis one with acute coronary insufficiency after a long history of angina pectoris and one with a hyperkinetic circulatory state due to severe anæmia The patients with occlusive coronary disease were all elderly men and the leukæmia was discovered as a result of a routine white count Whether the two diseases were coincidental or related is unknown The leukæmia was monocytic in three cases and myeloid in the other two

Argentaffinoma

In 1952 Biorck Axen and Thorson described the unusual association of pulmonary valve stenosis gross tricuspid incompetence and carcinoid of the small intestine with metastases in the liver in a boy of 19, a remarkable feature of the case was intense patchy and variable reddish blue cyanosis and attacks of flushing there was also a nine year history of asthma and diarrhoea In 1954 Thorson Biorck and Bjorkman reported seven definite cases of this interesting syndrome and concluded that the secretion of large quantities of serotonin (5 hydroxytryptamine) by the carcinoid and its metastases was responsible for the acquired pulmonary and tricuspid valve lesions as well as for flushing patchy cyanosis bronchospasm and diarrhoea The syndrome has excited considerable interest and a number of similar cases have been reported by others since (e g Bean *et al*, 1955)

Biochemically serotonin (5 hydroxytryptamine) has been demonstrated in high concentration in the serum and urine of patients with argentaffinoma of the small intestine (Pernow and Waldenstrom 1954) as well as in the tumour itself and its metastases (Lembeck 1953) Serotonin is inactivated by a lung enzyme—monoamine oxidase (Bradley *et al*, 1950)—which breaks it down to 5 hydroxyindoleacetic acid (5 H I A A) and an enormous increase of this substance has been found in the urine of patients with argentaffinoma (Page *et al* 1955) In a case of my own there was good evidence that serotonin was inactivated in the lungs because its concentration in the serum and plasma fell from 56 and 62 μg per cent respectively in samples from the pulmonary artery to 19 and 22 μg per cent respectively in samples obtained from the brachial artery (Goble Hay and Sandler 1955) It is not yet clear how serotonin causes fusion of the pulmonary and tricuspid valve cusps, but its inactivation in the lung explains why the valve lesions are right sided

Clinically the syndrome is easily recognised by anyone familiar with its manifestations The combination of the peculiar mottled or patchy cyanosis the attacks of flushing and bronchial asthma the diarrhoea large liver (from metastases) and signs of mild or moderate pulmonary and tricuspid stenosis are too characteristic to be mistaken for any other condition In my own case (a 33 year old woman) the pulmonary stenosis was of moderate degree (P A P 9/4 R V P 45/-5 C O 3 5 L/min at rest) and the tricuspid stenosis mild (presystolic pressure gradient 4 mm Hg) There was a two year history of blotchy erythema marked flushing and asthma attacks being precipitated by meals so that she became afraid to eat The primary tumour was removed from the ileum but there was little improvement owing to the extensive metastases in the liver and she died within six months of her first admission to hospital Necropsy confirmed the diagnosis Full details of this case are being reported by Goble *et al* (1956)

MYOCARDITIS DUE TO DRUGS

Certain therapeutic drugs have earned the reputation of being dangerous to the heart either by causing transient toxic myocarditis or by inducing ventricular fibrillation or asystole In the first group the best known are digitalis and emetine in the second choloroform adrenaline and potassium Toxic myocarditis due to drug allergy is in a different category and has already been discussed

DIGITALIS

Digitalis is undoubtedly the best example of a therapeutic drug that may cause dangerous myocardial poisoning

Pathology Buchner (1934) first demonstrated that necrotic myocardial lesions could be produced in animals (cats) by means of digitalis Dearing Barnes and Essex (1943) also working on cats produced focal necrosis cellular reaction and fibroblastic repair Similar necrotic lesions may be provoked by acetylcholine and by continuous direct vagal stimulation (Banting and Hall 1936 1937) and have been ascribed to coronary constriction In the belief that the lesions due to digitalis were caused by the activity of acetylcholine Kyser Ginsberg and Gilbert (1946) succeeded in

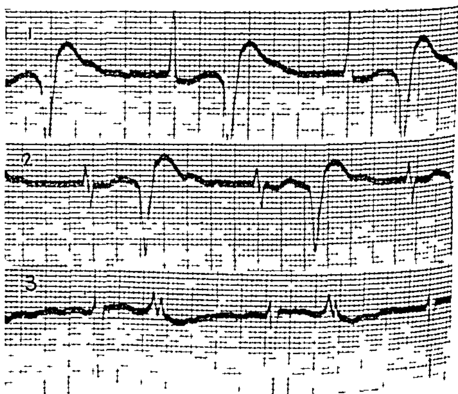


Fig 11 06—Electrocardiogram showing coupling from ventricular ectopic beats due to digitalis

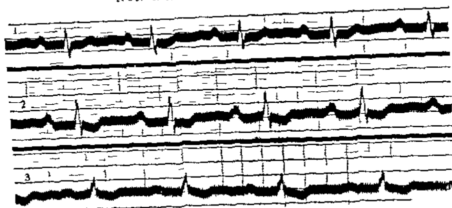


Fig 11 07—Electrocardiogram showing partial heart block due to digitalis

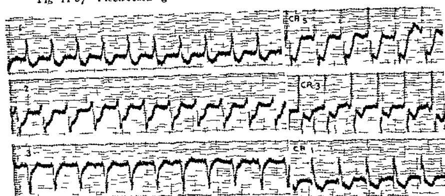


Fig 11 08—Electrocardiogram showing paroxysmal tachycardia due to digitalis

preventing them by the simultaneous administration of atropine or a coronary vasodilator such as theophylline Whether digitalis intoxication in man is characterised by similar patchy myocardial necrosis and whether this is mediated by vagal stimulation remain to be proved but it is a reasonable hypothesis Certainly the effect of acetylcholine is augmented in the presence of strophanthin or digitalis (Danielopolu 1946)

Clinical features Anorexia nausea or vomiting and diarrhœa usually give sufficient warning of digitalis overdosage but there may be no such indication when carditis from other causes is already present Disturbances of rhythm are common and include coupling due to premature ectopic beats (fig 11 06) nodal rhythm partial or complete heart block (fig 11 07) multiple ectopic beats atrial fibrillation paroxysmal tachycardia (fig 11 08) and sudden death from ventricular fibrillation

The electrocardiogram shows characteristic sagging depression of the RS T segment (fig 11 09) maximum in leads V_{4-6} when there is normal or increased left ventricular dominance or in leads V_1 when there is right ventricular preponderance The depression is transmitted chiefly to

lead V_L or V_F and thence to the appropriate standard lead according to the electrical position of the heart At first the peak of T remains upright but later becomes absorbed in a sharply depressed RS T segment, the Q T interval being shortened (fig 11 10) The electrocardiogram offers by far the most reliable evidence of digitalis saturation even when the patient denies having taken the drug

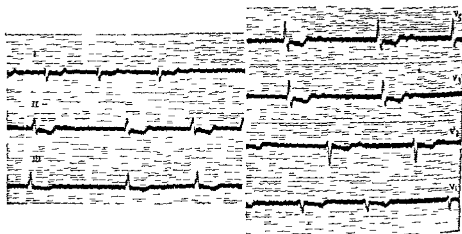


Fig 11 09—Electrocardiogram showing depression of the RS T segment due to digitalis

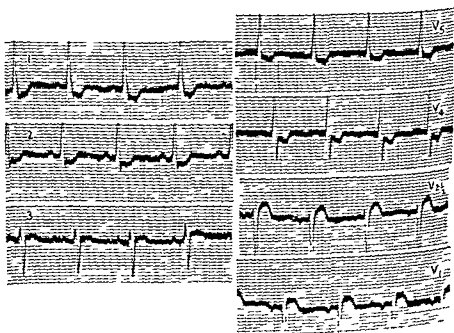


Fig 11 10—Shortening of the Q T interval due to digitalis Q Tc—0 3 sec

Treatment The best remedy apart from stopping digitalis is atropine but it is rarely necessary If the degree of intoxication appears dangerous however it may be given in doses of 0 5 mg four hourly for a day or two

EMETINE

Emetine is another therapeutic drug with a reputation for causing toxic myocarditis the chief danger being abnormalities of rhythm particularly ventricular fibrillation Emetine was used a great deal amongst British troops in the Mediterranean theatre during the second world war but ill effects on the heart were very rare if they occurred at all Patients receiving emetine however were always confined to bed throughout the course

Fatal cases of toxic myocarditis described in the literature received a total dose of 1 04 to 2 65 G of emetine over a period of two to six weeks (Brown 1935) Emetine is highly cumulative being excreted very slowly and the minimum lethal dose is said to be around 20 mg /kilo

OTHER DRUGS

Potassium when used in large single doses (8 to 16 G) to stop paroxysmal tachycardia or multiple ectopic beats or to differentiate between ischæmic and other causes of T wave inversion is undoubtedly dangerous and may cause sudden death from ventricular asystole preceded by increasing heart block and bundle branch block Spontaneous potassium poisoning may cause sudden death in uræmia (Marchand and Finch 1944) The electro cardiogram in such cases shows widened QRS complexes and tall peaked T waves (fig 11 11)

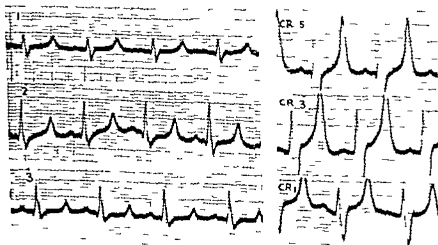


Fig 11 11—Widening of the QRS complex and accentuation of the T wave due to a high blood potassium in a case of uræmia The long Q T is due to hypocalcæmia

The normal serum potassium is 15 to 21 mg per cent (4 to 5.5 m eq per litre) It may be reduced in a variety of conditions including familial periodic paralysis diabetic acidosis ulcerative colitis idiopathic steatorrhœa, vomiting from interstinal obstruction and as a result of prolonged treatment with resins Electrocardiographic changes include flattening of the T wave, augmentation of the U wave, depression of the S T segment and prolongation of the P R Q T and Q U intervals (Perelson and Cosby 1949 Bellet *et al* 1950) The amplitude of T declines when the serum potassium is at 13 to 14 mg per cent U becomes prominent at 10 to 12 mg per cent and depression of the S T segment at about 8 mg per cent (Metzger and Blum 1950) Ectopic beats and perhaps other arrhythmias may result from these low potassium levels and McAllen (1955) found widespread myocardial fibrosis at necropsy in two cases

Adrenaline in large doses may excite ectopic beats or almost any change of rhythm except heart block Transient hypertension and inversion of the T wave in leads V_{4-6} are common Violent palpitations and substernal discomfort may occur and patients with ischæmic heart disease usually develop a severe attack of angina pectoris Clinical examples may result from errors in the dose of adrenaline administered or from spontaneous hyperadrenalism in cases of pheochromocytoma

Chloroform is an example of a group of drugs mostly anæsthetics which may cause sudden death from ventricular fibrillation especially in the presence of an excess of adrenaline

Nicotine as absorbed by heavy smokers may provoke ectopic beats and cause slight coronary and peripheral vasoconstriction and so aggravate angina pectoris hypertension and peripheral vascular disease *Barium chloride* causes ectopic beats

Alcohol is a vasodilator and in moderate amounts may benefit ischæmic heart disease on the other hand it may increase the work of the heart especially if the blood volume is temporarily raised Heavy drinkers may suffer from an inadequate supply of aneurin and may develop heart failure in consequence or their high carbohydrate low protein diet may lead to another form of nutritional cardiopathy as described on page 628 Finally under the influence of alcohol patients are apt to be careless of medical advice and may exert themselves more than they should

THE HEART IN ACUTE NEPHRITIS

Carditis accompanying acute nephritis (Whitehill *et al* 1939) and toxæmia of pregnancy (Szekely and Snaith 1947) is particularly interesting The chief clinical features are elevation of the venous pressure a tendency to develop acute pulmonary œdema general enlargement of the heart and inversion of the T wave in leads facing the surface of the left ventricle (Master Jaffe and Dack 1937) The degree of hypertension is often insufficient to explain these findings Nephritic œdema is usually present the blood volume is raised and the circulation time normal (Klein 1947)

That there may be some form of cardiopathy is suggested in certain cases by the behaviour of the cardiac output which may fail to rise as expected when the venous pressure is high moreover the Valsalva test yields a square wave response (Sharpey Schafer 1955) On the other hand

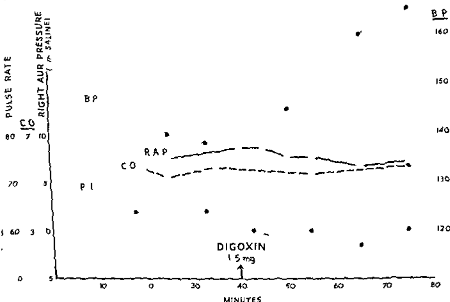


Fig 11 12—Graph illustrating a high right atrial pressure that is not reduced by digitalis in a case of acute nephritis There is a conspicuous rise of blood pressure and slight slowing of the pulse the cardiac output is unchanged

the lack of response to digitalis (fig 11 12) shows that the heart is not over loaded Histological examination of the heart muscle in fatal cases of acute nephritis presenting cardiac signs seldom reveals any structural abnor mality sometimes however the muscle fibres are dispersed by serous exudate lymphocytes and endothelial cells—even then there is little if any necrosis (Gore and Saphir 1948)

It is probable therefore that the raised venous pressure is mainly due to an increased blood volume from retention of sodium and water, and that as a rule the heart responds normally but that in certain instances cardiac function is impaired owing perhaps to biochemical rather than structural changes in the heart muscle, whether acute pulmonary œdema is a manifestation of left ventricular failure or whether it is due to a toxic or allergic effect on the pulmonary capillaries is not yet known

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CHAPTER XII

BACTERIAL ENDOCARDITIS

BACTERIAL or infective endocarditis means bacterial infection of any of the heart valves or of certain congenital anomalies of the heart or great vessels (bacterial endarteritis) It occurs in two main forms acute (malignant), due to infection with any of the pyogenic bacteria and subacute, due mainly to the *Streptococcus viridans* but many other organisms have been isolated from both types This broad classification is necessarily artificial, the course of the disease depending on the virulence of the organism and the resistance of the host There is no clear division between the two types and they are better considered as one disease

There is usually some underlying fault congenital (10 per cent) or acquired The most susceptible congenital anomalies are pulmonary stenosis bicuspid aortic valve ventricular septal defect and patent ductus arteriosus atrial septal defect is remarkably immune Any acquired valve lesion may become infected including syphilitic aortic incompetence (Martin and Adams 1938) and calcific aortic stenosis (Brink and Smith 1937) but old rheumatic valvulitis is to blame in 80 per cent of cases (Clawson 1948) In quite a number active rheumatic infection is still present when bacterial endocarditis is superimposed The most susceptible valve fault is mild mitral incompetence

PATHOLOGY

The lesion is superficial and is not a valvulitis in the sense that rheumatic endocarditis is bacteria invade the surface of a damaged or congenitally deformed valve and are encouraged by the formation of small superficial thrombi which provide an excellent culture medium Both in the natural disease and experimentally in dogs there appears to be a paucity of granulation tissue and of cellular reaction the microbes are not destroyed and healing does not take place Elsewhere in the body similar foci of bacteria are rapidly walled off by granulation tissue and the lesion is invaded by leucocytes the microbes are destroyed and the inflammation soon subside (Friedman Katz Howell *et al* 1938)

The macroscopic appearances vary according to the infecting organism, tending to be finely granular with streptococcus viridans ulcerative and hæmorrhagic with the hæmolytic streptococcus and pneumococcus proliferative with the gonococcus When associated with congenital defects the site of the vegetations depends upon the direction of blood flow through the defect thus in the maladie de Roger vegetations are found on the right side of the patent interventricular septum and on the wall of the right

ventricle opposite the defect with patent ductus arteriosus they are found at the pulmonary artery end Ulceration may lead to perforation of a valve cusp or sinus of Valsalva In old rheumatic cases vegetations may spread on to the endocardium of the left atrium (Thayer 1926)

The myocardium may show scattered focal lesions similar to those seen in isolated or toxic myocarditis or small collections of lymphocytes or lymphocytes and polymorphs known as Bracht Wachter bodies (Bracht and Wachter 1909) The latter are believed to be embolic in origin and represent a local inflammatory reaction to bacterial nests (Perry 1936) They are the non suppurative counterpart of the miliary abscesses seen in staphylococcal cases Saphir Katz and Gore (1950) found myocardial lesions in all of 76 fatal cases they included emboli micro infarcts peri vascular infiltration micro abscesses interstitial infiltration and myo cardial necrosis

OCCURRENCE

Bacterial endocarditis accounts for about 2 per cent of all cases of organic heart disease (White 1937) and for 9 per cent of all deaths from heart disease (Clawson 1948) It may occur at any age but is most common in young adults of either sex Auricular fibrillation occurs in only 2 5 per cent of cases (McDonald 1946) presumably because it is not a feature of the congenital lesions mentioned is uncommon in rheumatic aortic valve disease and occurs late in the life history of patients with mitral stenosis There is no evidence that the two conditions are mutually antagonistic

CLINICAL FEATURES

Patients may present themselves with cardiac symptoms pyrexia of un known origin anaemia a cerebral vascular lesion subacute rheumatism *nephritis* broncho pneumonia or with other patterns which depend upon the nature of the invading organism the underlying cardiac lesion and the caprice of the disease process At the onset symptoms are often ascribed to *influenza* but fail to clear up A history of dental sepsis or recent tooth extraction is obtained in 48 per cent of cases (Gates and Christie 1951) The diagnosis rests upon the combination of a variety of signs which will be considered individually

Cardiac abnormalities There should be evidence of one or other of the various underlying valve lesions or congenital defects already mentioned especially mitral or aortic incompetence and if there are no abnormal auscultatory signs of heart disease the diagnosis is rarely tenable The development of a new valve lesion or of the whining diastolic murmur and thrill of a perforated aortic cusp may be highly suggestive

Toxic myocarditis is not uncommon and may cause heart failure and death whether the infection yields to treatment or not Its importance has been more widely recognised since the introduction of penicillin (Saphir

Katz and Gore 1950) Heart failure occurs most frequently towards the end of the course of antibiotic treatment or during convalescence and was detected in no less than 63 per cent of the 442 cases analysed by Cates and Christie (1951)

Pyrexia Acute cases are always febrile subacute cases are always febrile at some stage in the disease but bouts of fever may alternate with afebrile periods The fever is irregular in type usually low grade or moderate in degree and may continue for weeks months or years

Anæmia Anæmia nearly always develops early and is already present in about three quarters of the patients when first seen It is indeterminate in type being normocytic and orthochromic, even when associated with hæmolytic infections The red cells may be reduced to about three million and the hæmoglobin to about 60 per cent, giving a normal colour index Stained films and bone marrow samples reveal no specific features If microcytic hypochromic anæmia is found the diagnosis should be doubted for iron deficiency anæmia itself may cause many of the signs and symptoms of bacterial endocarditis e g functional systolic murmurs at the base or the apex of the heart splenomegaly petechiæ red cells in the urine, and even low grade pyrexia

The white count is variable It may be normal on the other hand there may be moderate leucocytosis or leucopenia Leucocytosis is usually associated with acute septicæmic cases normal or leucopenic counts with subacute infections

Splenomegaly The spleen is usually palpable It may be soft as in typhoid when due to septicæmia it may enlarge rather suddenly as a result of splenic infarction when it is tender it may be firm in subacute cases or it may be so large as to cross the mid line in chronic cases

Petechiæ Petechiæ are common and sometimes appear in successive crops They may be seen under the nails in the ocular fundi in the conjunctivæ or anywhere in the skin or mucous membranes Under the nails they resemble small splinters (Horder 1926) in the fundi they may have white centres of exudate, in the skin they must be distinguished from minute telangiectases—Campbell de Morgan s spots Petechiæ in successive crops or otherwise are in no way diagnostic of bacterial endocarditis They are due to capillary hæmorrhage and may occur in any condition in which the capillaries are suitably damaged including most forms of septicæmia acute rheumatic fever (especially when associated with acute glomerulonephritis) and severe anæmia In bacterial endocarditis the capillary lesion may be due to toxins, to allergy or to anæmia

Increased capillary fragility may be demonstrated by the capillary resistance test

A cuff is placed on the upper arm inflated to a pressure of 50 mm. of mercury and maintained for five minutes alternatively a pressure of 80 mm of mercury may be maintained for three minutes The arm below the cuff is then inspected. Most normal subjects are unaffected but some develop a few tiny petechiæ in the

ante cubital fossa The result of the test may be expressed as slightly moderately considerably or grossly positive or as negative the four positive grades representing transitions from a few tiny hæmorrhages to gross purpura

The test may be positive or negative in bacterial endocarditis when spontaneous petechiæ are present When positive it is well to make sure that vitamin deficiency is not responsible or to cover this possibility by giving adequate doses of ascorbic acid rutin and crude vitamin P

Small hæmorrhagic pustules in the skin may occur in the acute pyogenic forms of bacterial endocarditis and are embolic in origin

Clubbing of the fingers (and toes) Clubbing occurs in about half of the subacute cases but as it takes at least 3 to 6 weeks to develop it is rare in malignant endocarditis Early clubbing may be recognised by noting congestion and thickening of the nail fold and loss of the normal angulation between the nail fold and the base of the nail Slight clubbing should be interpreted with caution however for it may occur in many conditions including active rheumatic carditis Conspicuous clubbing on the other hand provides excellent supportive evidence of bacterial endocarditis if cyanotic congenital heart disease pulmonary abscess bronchogenic carcinoma and a congenital origin can be excluded

Nodes Osler s nodes are small transient erythematous lesions about the size of a pea lasting a few days and vivid pink in colour when fresh bluish when fading often with a darker centre they are raised palpable and tender and may be found particularly on the pads of the fingers and toes on the sides of the fingers or on the thenar or hypothenar eminences (Osler 1909) They are due to infected cutaneous emboli and the responsible organism may sometimes be cultured from them

More important perhaps because more common are larger deeper nodes which vary from the size of a pea to that of a grapefruit They are red painful hot and tender, may occur anywhere in the limbs and may be mistaken for osteomyelitis or periostitis When a lesion involves the finger it closely resembles an ordinary infected pulp it is non suppurative however and disappears in about a week if left alone Cultures from the inflamed tissue may yield *Streptococcus viridans* Red tender macules are equally characteristic and even more common and may also yield positive cultures from biopsies

Emboli In addition to the minute emboli which cause white centred petechiæ and the nodes just mentioned larger emboli may block any artery —cerebral, visceral, or peripheral They are more common in the radial ulner, posterior tibial and dorsal artery of the foot than in the axillary or femoral artery because their size is limited For this reason peripheral emboli are often symptomless and are only discovered by those who look for them In cases of suspected bacterial endocarditis the peripheral vessels should always be palpated and their patency noted for future reference In the series of 442 cases reported by Cates and Christie (1951) a major arterial embolism occurred in 35 per cent

Mycotic aneurysm Ulceration or degeneration of the wall of an artery due to *local inflammation from an infected embolus lodging within the vessel* or in its vasa vasorum may result in the formation of a small aneurysm Severe hæmorrhage results from rupture of a mycotic aneurysm and may prove fatal if cerebral or visceral

Pulmonary emboli When bacterial endocarditis involves the pulmonary or tricuspid valve or when it is associated with a left to right cardiac shunt as in patent interventricular septum emboli may be flung into the pulmonary circulation Numerous small pulmonary infarcts result and may give rise to a clinical picture resembling recurrent or subacute hæmorrhagic bronchopneumonia

Renal lesions The various renal lesions that may occur in bacterial endocarditis represent almost every aspect of the disease

(1) An embolus lodging in a small renal artery leads to simple infarction of the kidney with hæmaturia or without signs or symptoms

(2) Minute bacterial emboli may cause embolic nephritis which in greater or less degree is found in the majority of cases Only some of the glomeruli are involved rarely more than 60 per cent and most of these have some of their capillary loops intact so that the tuft is not entirely avascular and the health of the tubules is not seriously threatened Affected capillaries are converted into a hyaline mass and red cells may be found in the capsular space and in the urine Embolic nephritis does not cause renal failure because a sufficient number of glomeruli are always spared (Baehr 1921)

(3) In acute pyogenic forms of bacterial endocarditis particularly when pneumococcal or staphylococcal in origin miliary abscesses may be found in the substance of the kidney

(4) Petechiæ due to simple capillary hæmorrhage may occur on the surface of the kidney in the absence of embolic nephritis They are then similar to those found in the pericardium pleura and skin

(5) Acute diffuse glomerulo nephritis may occur as with other streptococcal infections and may progress to renal failure but not more than 5 to 10 per cent of all cases take this course

(6) Simple congestion of the kidney may result from heart failure and give rise to albuminuria and to a few red cells in the urine

It will be appreciated that these six types of renal lesion represent thrombotic emboli benign bacterial emboli septic emboli simple hæmorrhage toxæmia or allergy and heart failure respectively, and that nearly all the features of bacterial endocarditis may be understood in terms of these six factors

Changes in the ocular fundus Simple petechiæ like those in the skin are fairly common Occasionally they have white centres and may be embolic in origin It should be understood that these white centres represent exu

date and that identical lesions may be seen in other conditions particularly leukæmia and malignant hypertension The exudate may be surrounded by hæmorrhage or may be to one side of it Embolism of the central artery of the retina or of one of its main branches may cause complete or partial loss of vision but is fortunately rare Finally papillædema or papillitis with or without widespread hæmorrhages and exudates is not uncommon when there is diffuse glomerulo nephritis the appearances resembling those of malignant hypertension

DIAGNOSIS

It is emphasised that pyrexia anæmia splenomegaly petechiæ and diffuse glomerulo nephritis may occur wherever the site of the cardiac lesion that systemic emboli mycotic aneurysms nodes and embolic nephritis signify left sided lesions e g aortic or mitral valve disease that multiple hæmorrhagic infarcts in the lungs are the prerogative of right sided valve lesions and of left to right congenital shunts such as patent ductus and maladie de Roger (Barker 1949)

Clinically bacterial endocarditis should be considered in all cases of unexplained fever with suspicious auscultatory signs in the heart If an indeterminate anæmia is also present a determined search should be made for other evidence if splenomegaly petechiæ and red cells in the urine are added the diagnosis becomes probable but is still uncertain On the other hand clubbing of the fingers nodes peripheral emboli mycotic aneurysm nephritis and characteristic fundal changes may each one of them be diagnostic of bacterial endocarditis when associated with fever and an appropriate cardiac lesion

The diagnosis is confirmed by a positive blood or bone marrow culture Six tubes are usually set up from each sample and 4 to 6 samples should be obtained at different times preferably when the temperature is high before a negative result is accepted It should be pointed out however that blood cultures from patients with pyorrhœa or with dental abscess may grow *Streptococcus viridans* when the specimen is obtained after chewing so that the diagnosis of bacterial endocarditis should never rest on a positive blood culture alone

NATURAL COURSE

Untreated patients with acute infection die in a matter of days or weeks usually from septicæmia or from the effects of embolism those with sub acute infection usually live for months and occasionally for years bouts of fever with exacerbation of signs and symptoms alternating with afebrile quiescent phases described by Libman as bacteria free periods Death may result from heart failure cerebral or other visceral embolism hæmorrhage uræmia or other causes According to Libman and Friedberg (1941) about 3 per cent of all patients recover spontaneously but Lichtman (1943) found that only 1 per cent of 2 596 cases collected from the literature so recovered

PROGNOSIS

Penicillin and streptomycin have radically altered the course of bacterial endocarditis for the infection can now be controlled in 90 per cent of cases However about 25 per cent still die during or shortly after treatment *mostly from heart failure This high mortality may be due to the frequency* of serious toxic myocarditis and to the relatively rapid increase in severity of valve lesions particularly aortic or mitral incompetence Uræmia accounted for only 6 per cent of the 131 deaths in the combined hospitals series reported by Christie (1948) emboli for 11 per cent and hæmorrhage for 8 per cent The most important factors influencing the mortality rate proved to be the presence and degree of heart failure the duration of the infection and the nutritional state of the patient

Relapses are common in inadequately treated cases, but should not exceed 10 per cent in patients who have received at least 0 5 mega unit of penicillin daily for a minimum period of 28 days Nearly all those who *relapse do so within one month of ceasing treatment* The frequency of recurrence (as distinct from relapse) is not yet known

TREATMENT

Prophylactic Surgical repair of patent ductus arteriosus not only cures the defect but protects the patient from infective endarteritis Repair of coarctation of the aorta may be less successful in the second respect because infection may yet complicate an associated bicuspid aortic valve *It is not* expected that surgical relief of pulmonary stenosis will reduce the frequency of bacterial endocarditis in that disease

Dental hygiene is particularly important in all patients who have congenital heart disease or chronic valve disease Tooth extractions tonsillectomy and other E N T operations should be covered by 300 000 units of procaine penicillin twice daily for five days or perhaps 600 000 units daily A single *intramuscular injection* of benzathene penicillin 600 000 units the day before tooth extraction may also suffice but awaits longer trial

Chemotherapy Sulphonamides have proved disappointing and although they may temporarily sterilise the blood stream and lower the temperature they rarely cure the disease Of 489 cases treated with sulphonamides alone, only 4 per cent recovered (Lichtman 1943)

The situation has greatly improved since the introduction of penicillin Patients should be treated early as soon as the diagnosis is *clinically* probable without waiting for positive results of blood cultures Every effort should be made to counter malnutrition and a blood transfusion should be given if there is serious anæmia

The minimum dose of penicillin is 0 5 mega unit daily given *in divided* doses of 60 000 units three hourly 80 000 units four hourly or 120 000 units six hourly and continued for twenty eight days Nothing less than

this will suffice and larger doses averaging 2 mega daily, prolonged for six to eight weeks are preferred (Cates and Christie 1951) One of my patients was not controlled until she received a million units three hourly and a total of 250 million units If the resistance of the organism is known so much the better but even then the optimum dose cannot be calculated exactly because it depends partly on the physical properties of the lesion Swift and maintained clinical response is the only reliable criterion by which to judge the correct dose If however the resistance of the organism is known to be more than eight times that of the standard test strain of Oxford staphylococcus the dose of penicillin should certainly be increased proportionately (Christie 1948) If the coefficient of resistance is 10 not less than 100 000 units three hourly will suffice if 20 then at least 200 000 units three hourly will be necessary—and so on (Baehr and Gerber, 1947) Peak (15 to 30 minutes after intramuscular injection) or constant (with the intravenous drip method) blood serum levels of penicillin expressed in units per ml may also be measured and checked against tables giving the expected level for the dose employed Peak levels should range from 2 to 25 units per ml with doses of 60 000 to 500 000 units intramuscularly constant levels between 1 and 10 units per ml with daily doses of 500 000 to 4 million units

A practical method of arriving at the right dosage that has given good results for many years is to start with 100 000 units four hourly and to double the dose every second day until the fever abates the dose to which the patient responds is thus known and is promptly doubled for maintenance purposes and continued for six weeks This method has the advantage of testing the sensitivity of the organism to penicillin *in vivo* and ensuring an adequate therapeutic maintenance dose The theoretical objection that it might breed penicillin resistant organisms has not been substantiated in practice

To avoid the discomfort of frequent needling there is an increasing tendency to give massive doses of penicillin (0 25 to 0 5 mega unit) three or four times daily As these massive doses have a penetrating power denied to more modest quantities there is something to be said for this method but they should not be given too infrequently

Another way of avoiding such frequent injections is to use one of the longer acting penicillins such as procaine penicillin As an aqueous suspension this may be injected intramuscularly in doses of 600 000 units twice daily It should never be u ed at the start however and is only advised later in cases that have responded quickly and dramatically to the minimum daily dose of sodium penicillin G

Finally the blood level of penicillin may be increased up to fourfold by the oral administration of certain substances such as benzoic acid (Bronfenbrenner and Favour 1945) sodium benzoate or caronamide (4 carboxyphenylmethane sulphonanilide) which interfere with penicillin excretion by the renal tubules The dose of each of these substances is 2-3 G four

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Heart failure should be treated in the customary fashion but the prognosis is grave in these cases

Diffuse glomerulo nephritis may be mistaken for a relapse of bacterial endocarditis If the renal function is impaired the blood level of penicillin may rise considerably and thus aid the primary treatment unfortunately, however the nephritis usually proves fatal According to Spain and King (1952) diffuse glomerular nephritis rarely occurs if treatment is started within the first two months of the illness

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hourly (Boger *et al*, 1948) Caronamide may be combined with sodium benzoate with some advantage and is a valuable adjunct to treatment in highly resistant cases Probenecid (Benemid) now seems to be replacing caronamide the dose is 0 5 G six hourly

Treatment of relapses or resistant cases If the previous course of treatment was inadequate in dosage or duration the standard course of 2 mega units daily for six weeks should be instituted but if a relapse follows adequate treatment every effort should be made to culture the organism and to determine its sensitivity to penicillin If its resistance is not greater than eight times the standard the dose of penicillin should be doubled and treatment should be continued for six weeks If the coefficient of resistance is greater than 8 the dose of penicillin should be increased proportionately If the organism is highly resistant or if it has not been isolated and the infection remains uncontrolled streptomycin may be tried The dose is 1 G twice daily for two weeks followed by 1 G daily for four more weeks Caronamide does not influence the blood level of streptomycin, for the latter is excreted by the glomeruli

Combined penicillin and streptomycin treatment is advised for entero coccal infections (Hunter 1947 Geraci and Martin 1954) The dose of peni cillin in these cases should be at least 10 million units daily (Hunter 1953)

Innumerable reports of resistant cases of bacterial endocarditis caused by a wide variety of organisms have appeared in the literature in recent years and the majority have responded in the end to one or other of the newer antibiotics when given in sufficient doses To review all these reports would be profitless The resistant case is a bacteriological problem The organism should be identified and its sensitivity to all available anti biotics tested in the laboratory treatment may then be instituted on a proper foundation

Toxic reactions of penicillin Apart from local pain from subcutaneous or superficial intramuscular injections and phlebothrombosis from intra venous injections the only toxic manifestations which can be attributed to penicillin are fever and urticaria Fever was common when crude penicillin was used but is rarely seen nowadays Urticaria develops in about 5 per cent of cases and may be extreme soft tissue œdema and hydrarthrosis are occasionally associated This allergic reaction is alleviated by adrenaline and by the antihistamine group of drugs Penicillin may be continued in mild cases but may have to be stopped if the reaction is severe or the dose may have to be reduced

The chief toxic effect of streptomycin is on the vestibular nerve loss of the sense of balance may be permanent if heavy doses are continued after giddiness has developed A conservative dose of 1 G daily however may be continued in the presence of minor vestibular symptoms if the latter are controlled by means of antihistamine drugs

Other considerations An infected ductus should be controlled by peni cillin then ligated as soon as the patient is fit enough

CHAPTER XIII

PERICARDITIS

THE features of pericarditis depend upon its etiology the presence or absence of effusion the nature and hydrostatic pressure of such effusion and the development or otherwise of constriction in chronic or adhesive cases

ETIOLOGY

Pericarditis may be benign, rheumatic tuberculous pyogenic allergic traumatic uræmic or secondary to myocardial infarction malignant growths may invade the pericardium hæmopericardium may result from rupture of a syphilitic or dissecting aneurysm from perforation of a myocardial infarct or ventricular aneurysm or from stab or gun shot wounds of the heart hydropericardium may complicate congestive heart failure or myxœdema sometimes the etiology is obscure All these types have their own special characteristics which will be described subsequently but they have also certain features in common

DRY (FIBRINOUS) PERICARDITIS

All varieties of pericardial inflammation may present in this form The diagnosis rests on three cardinal signs pain pericardial friction and a specific electrocardiographic pattern Disturbances of temperature pulse rate sedimentation rate etc of course may occur but are of little help in diagnosis

Pain Capps (1932) found that the pericardium was insensitive to stimuli calculated to produce pain except in that part of it roughly its lower third which is supplied by the phrenic nerve It follows that pericarditis should be painless unless the pain has phrenic distribution or unless it is pleural in type from secondary involvement of that structure In fact this is only partly true in many cases there is no pain in some pain is referred to the neck or shoulder tip in others it is precordial and pleural in type catching the breath on inspiration or on coughing but not infrequently the pain has none of these characteristics being præcordial constant sharp in quality and uninfluenced by respiration pericardial pain of this type may be aggravated by rotating the trunk or by swallowing (McGuire Kotte and Helm 1954)

Pericardial friction Friction sounds may be heard anywhere over the heart according to the site and nature of the pathological process but are most common at the left sternal border in the fourth intercostal space over the area of maximum cardiac dullness where the pericardium lies in contact with the chest wall They are superficial rough or smooth loud or

soft their timing is peculiar being out of step with the heart sounds Sometimes they are confused with the to and fro murmur of aortic valve disease or with artificial stethoscopic sounds sometimes they escape detection Pleuro pericardial friction can usually be distinguished by its relationship to respiration

Electrocardiographic changes A diagnostic electrocardiographic T_2 pattern first described by Porte and Pardee (1929) may be found in the majority of cases of genuine pericarditis whatever the etiology and whether

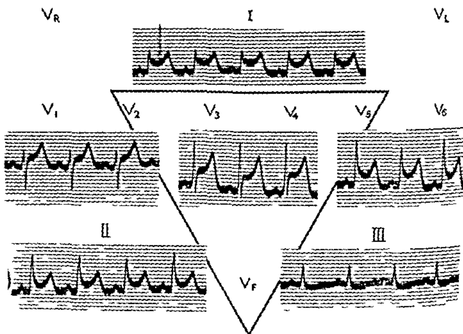


Fig 13 01—Electrocardiogram showing the early phase of the pericardial T_2 pattern This graph is atypical in that the R T segment is not elevated in lead 3

or not there is effusion (Wood 1937) It develops in two stages early and late the changes usually appearing in all leads and therefore especially in lead 2 In the early phase (fig 13 01) the RS-T segment is elevated but retains its natural concavity Within a few days it regains the iso potential level or becomes depressed and the T wave becomes flattened diphasic, or inverted (fig 13 02) QRS remaining unchanged throughout or losing voltage When the inflammation subsides the graph returns to normal except when a tuberculous pericarditis merges into the chronic constrictive form, when flat or inverted T waves and low voltage QRS complexes become permanent The T pattern may only be appreciated in serial electrocardiograms, because changes may be confined to leads 1 and 2 in one record, and to leads 2 and 3 in another Similar appearances are seen in all chest leads and may be found when limb leads are normal (fig 13 03)

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Fig 13 02—Electrocardiogram showing the later phase of the pericardial T_2 pattern case of pyogenic pericarditis secondary to bronchopneumonia

Both early and late stages appear to be due to alterations in the bio physical properties of the sub epicardial myocardium, whether or not there are recognisable structural changes (Kisch *et al* 1940) The early pattern of generalised pericarditis may be distinguished from that of myocardial infarction by the absence of a conspicuous Q wave by the preservation of the upward concavity of the RS T segment and by the occurrence of maximum RS T deviation in lead 2 (cf T_1 and T_3 types in myocardial infarction) When pericarditis is localised however changes may be maximum in leads 1 or 3 (Burchell Barnes and Mann 1939) The later stage

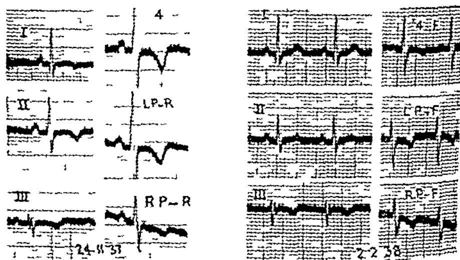


Fig 13 03—Electrocardiogram showing late changes due to pericarditis in the second record (2nd February 1938) they are limited to the chest leads

may be confused with isolated myocarditis myxœdema carbon monoxide poisoning severe anæmia and most of the cardiopathies described in the previous chapter On the other hand the characteristic initial phase, the changing picture in serial graphs and the clinical features of the case usually make the diagnosis easy

PERICARDIAL EFFUSION

Fluid in the pericardial sac may be a simple transudate (hydropericardium) a straw coloured sterile exudate a purulent exudate or blood (hæmopericardium) It may disturb the patient in one or more of four ways (1) stretching of the pericardium may induce præcordial discomfort (2) large effusions exerting pressure on surrounding structures especially on the bronchi and lungs may produce reflex cough and dyspnœa (3) if the fluid is purulent there may be constitutional effects similar to empyema, (4) as the pressure rises in the pericardial sac cardiac filling is hampered the pressure rises in both venous systems the ventricular stroke output diminishes and the blood pressure tends to fall The raised venous

pressure is partly beneficial for it aids cardiac filling the diminished stroke volume is countered by tachycardia reflex vasoconstriction serves to maintain the blood pressure (Stewart Crane and Deitrich 1938) When these compensatory adjustments fail to meet the circulatory demands the situation becomes critical (cardiac tamponade) There is reason to believe that cardiac tamponade seriously interferes with the coronary blood flow not only because the cardiac output is reduced and the blood pressure low but because the pressure gradient between the aorta and coronary circulation is significantly reduced The myocardium appears to suffer accordingly and true heart failure may result This may explain those cases that fail to recover after decompression and suggests that tamponade should be regarded as a medical emergency

Clinically the *pulse* may be normal small or paradoxical according to the intra pericardial pressure During inspiration descent of the diaphragm stretches the already tense parietal pericardium and increases the pressure within it cardiac filling is then impaired and the stroke output and pulse pressure fall As in constrictive pericarditis it is easier for the heart to increase its output by means of tachycardia than by raising the venous filling pressure

The venous pressure varies directly with the intrapericardial pressure and may rise appreciably during inspiration (Kussmaul s sign) The jugular pulse usually shows a rapid *v* descent and conspicuous *y* trough as in Pick s disease

Effusions in excess of 250 ml may be detected by *percussion* Dullness may be elicited in the second left space when the patient lies flat to the left of the apex beat when the latter can be located in the xiphisternal angle and to the right of the sternum in the 4th and 5th intercostal spaces (Rotch s sign 1878)

Auscultation reveals pericardial friction in the majority of instances even with gross effusions The first heart sound is soft because late diastolic ventricular filling is virtually at a standstill and the atrio ventricular valves are therefore more or less closed before the ventricles contract the second sound is soft because the blood pressure is low The fluid layer between the heart and chest wall may also damp the sounds but this is less certain Theoretically an accentuated third heart sound might be expected in view of the rapid ventricular filling in early diastole but it is rarely heard

Dullness to percussion and bronchial breathing at the left base usually attributed to collapse of the lung (Ewart 1896) are more likely to be due to associated pleural effusion at least in rheumatic cases (Thomas Besterman and Hollman 1953)

Fluoroscopy reveals a large relatively still cardiac silhouette with the natural contours of individual chambers obliterated (fig 13 04) It is doubted whether any of the special radiological points that have been said to favour effusion are really tenable e g short vascular pedicle divergent vascular shadows at the base change of shape with alteration of posture

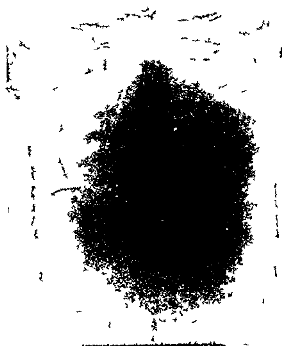
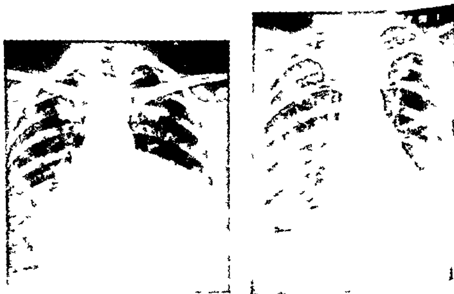


Fig 13 04—Skiagram of a case of pericardial effusion



(a) Before treatment (b) Two weeks later

Fig 13 05—Gross pericardial effusion

acute right cardio phrenic angle and convex posterior inferior cardio phrenic angle in the first oblique position (Besterman and Thomas 1953) Rapid changes in the size of the cardiac shadow are more reliable (fig 13 05) but even these may be seen in cases of acute dilatation of the heart with rapid recovery Since more accurate methods of diagnosis have been adopted there have been many surprises the more common error has been to mistake pericardial effusion for cardiac enlargement but the reverse has also been true

There are three good ways of determining the presence and degree of pericardial effusion—*cardiac catheterisation* angiocardiography and paracentesis If a cardiac catheter is looped in the right atrium its tip may be



Fig 13 06—Catheter looped in the right atrium proving the absence of pericardial effusion

rotated laterally and guided up and down the lateral wall of the right atrium When there is no effusion the tip of the catheter is then separated from the translucent lungs only by the thin wall of the right atrium (fig 13 06) When there is pericardial effusion however the tip of the catheter is separated from the lungs by an opaque band of fluid (Wood 1950 1951) If 10 to 20 ml of diaginol are injected rapidly through the catheter when its tip is directed upwards against the lateral wall of the right atrium and a film is exposed towards the end of the injection, the degree of effusion can be estimated accurately (fig 13 07) Routine *angiocardiography* (Williams and Steinberg 1949) reveals the degree of pericardial effusion with greater precision (fig 13 08) but may be undesirable when the alternative diagnosis is severe heart failure *Paracentesis* may prove the presence of effusion but only indicates its degree if all the fluid is removed or if sufficient air is introduced The safest of these three methods is

atrial catheterisation This does not, of course, distinguish pericardial effusion from gross dilatation of the left atrium

The *differential diagnosis* of pericardial effusion includes any general cardiac enlargement of uncertain nature heart failure from rheumatic carditis or any of the more obscure cardiopathies described in Chapter XI and certain congenital anomalies such as Ebstein s disease Under the clinical circumstances the best indication of pericardial effusion is a friction rub and the best evidence of cardiac dilatation is loud diastolic gallop rhythm A *paradoxical pulse certainly favours* effusion but too much reliance should not be placed on Kussmaul s sign the presence or absence of a palpable cardiac impulse the intensity of the heart sounds or inverted T waves in the electrocardiogram for all these may occur in either condition



Fig 13 07—Pericardial effusion seen beyond the right atrial border which is delineated by the tip of a looped catheter through which a jet of diodone has been injected

In addition to the three semi radiological methods of diagnosis described above certain physiological tests may prove useful although they have not been tested sufficiently yet These include Valsalva s manœuvre and the effect of alterations of posture on the cardiac output and therefore on the blood pressure pulse rate forearm blood flow and digital pulse In pericardial effusion the physiological response to the Valsalva manœuvre should be normal i e the period of strain should be followed by a rise of blood pressure and slowing of the pulse whereas in heart failure these changes do not occur Tilting the patient foot down lowers the venous pressure in pericardial effusion this should lower the cardiac output and so diminish the blood pressure and pulse pressure increase the heart rate reduce the forearm blood flow and diminish



Fig 13 08—Angiocardiogram demonstrating pericardial effusion

the digital pulse in heart failure, lowering the venous pressure increases the cardiac output and therefore has the opposite effect on the phenomena mentioned The essential principle underlying all physiological tests for pericardial effusion is that the heart behaves normally (Isaacs Berglund and Sarnoff 1954) whereas *cardiopathies with considerable cardiac dilatation* are overloaded

Cardiac catheterisation in both pericardial effusion and most of the obscure cardiopathies reveals that pulmonary venous and left atrial pressures are raised to just about the same level as the right atrial pressure in Ebstein s disease of course this is not so

Treatment The object of treatment is to prevent death from cardiac tamponade and is achieved by avoiding therapeutic agents that may lower the venous pressure such as mersalyl a low sodium diet and venesection and by decompression if necessary In practice it is rarely necessary to tap a pericardial effusion for critical tamponade is rare in medical cases The combination of a small pulse venous pressure over 10 cm of water at 90 degrees and systolic blood pressure below 90 mm Hg provides the necessary indication Paracentesis may be carried out to the left of the apex beat, or at any point where there is reason to believe there is plenty of fluid If the needle touches the heart forcible pulsation can be felt and it should be withdrawn a little or inserted elsewhere with due care the risk of causing hæmopericardium from puncturing a coronary vessel is small Fluid may also be removed if purulent or if untoward symptoms are caused by pressure on surrounding structures Traumatic hæmopericardium which is responsible for many cases of tamponade requires surgical evacuation and repair of the underlying injury

CHRONIC CONSTRICTIVE PERICARDITIS

Although Richard Lower described the paradoxical pulse and calcified pericardium as early as 1669 he was not in a position to grasp their full significance and it was Chevers who really drew attention to the disease giving an excellent account of it with considerable understanding of the circulatory dynamics involved in 1842 The term Pick s disease is unfortunate for Pick (1896) merely emphasised the accompanying pseudo cirrhosis of the liver and because priority undoubtedly goes to Chevers The issue is best avoided by adhering to the descriptive title—chronic constrictive pericarditis

Morbid anatomy The condition may be regarded as a complication of the healing process following tuberculous and perhaps certain other forms of pericarditis the fibrous tissue laid down so extensively in the active phase contracting on maturation and limiting diastolic expansion of the heart Calcium is often deposited in large quantities and the whole heart may become encased in stone

Etiology Tuberculosis accounts for at least three quarters of the cases and may still be active when constriction first develops The

bacteria appear to be responsible for a few and the cause is uncertain or unknown in the remainder None are rheumatic (White 1935) Some regard tuberculosis as the sole cause of chronic constrictive pericarditis (Andrews Pickering and Holmes Sellars 1948)

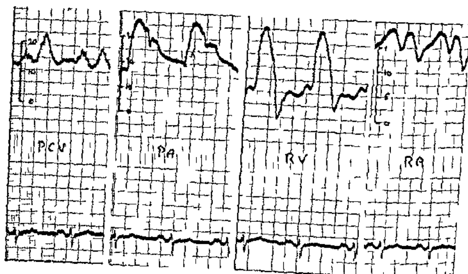


Fig 13 09—Intracardiac pressure pulses from a case of Pick s disease

Hæmodynamics

The essential physiological fault in Pick s disease is inadequate cardiac filling. It is uncertain to what extent ventricular contraction is also hampered but that it is so in some measure can scarcely be doubted The rigid limit imposed on diastolic filling is more or less the same for both ventricles so that the rise of pressure in the two venous systems is always similar if not identical This was true in all of eight consecutive cases that we have investigated and in a series of six cases reported by Dexter s group (Sawyer *et al*, 195-) The elevated atrial and venous pressures usually measure between 10 and 20 mm Hg above the sternal angle (fig 13 09) As a rule the dominant wave is the y descent and trough (fig 13 10) This represents the sudden fall in venous pressure that follows the opening of the tricuspid valve when blood pours into the momentarily relaxed right ventricle Owing to the unyielding pericardium the right ventricle is filled to its maximum

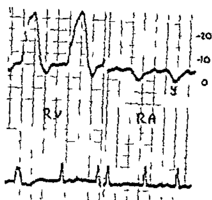


Fig 13 10—Typical right atrial and right ventricular pressure pulses in a case of Pick s disease showing conspicuous y troughs

capacity very quickly and both right ventricular and right atrial diastolic pressures therefore rise again smartly The right ventricular pressure pulse is characterised by a conspicuous dip in early diastole which is the counter part of the y trough in the venous pulse The same phenomenon may be recorded in left atrial and left ventricular pressure pulses (fig 13 11) Typical tracings have been published and discussed by Bloomfield *et al* (1946) Eliasch Lagerlof and Werko (1950) Hansen *et al* (1951) and McKusick (1952)

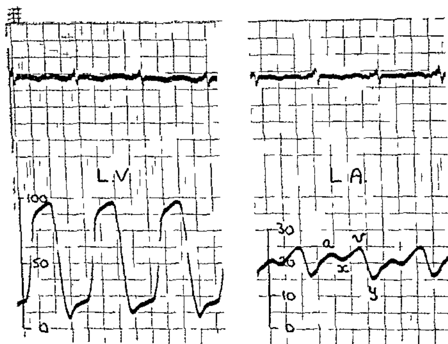


Fig 13 11—Left atrial and left ventricular pressure pulses from a case of Pick s disease

Since the stroke output is strictly limited and more or less fixed alterations of cardiac output per minute depend chiefly on changes in heart rate (Stewart and Heuer 1939) Raising or lowering the venous pressure makes relatively little difference Since maximum filling is accomplished very quickly doubling the heart rate may almost double the minute output

The Valsalva manœuvre may give rise either to a normal or to a square wave response (fig 13 12) and may therefore fail to distinguish constrictive pericarditis from heart failure It is presumed that an intrathoracic pressure of 40 mm Hg may fail to compress the calcified box that encloses the heart The assumption that cases giving a square wave response are really in a state of myocardial failure is unwarranted on the other ha

is not denied that true heart failure may occur, and can sometimes be demonstrated post operatively

Other physiological phenomena such as Kussmaul's sign and pulsus paradoxus are discussed with the physical signs

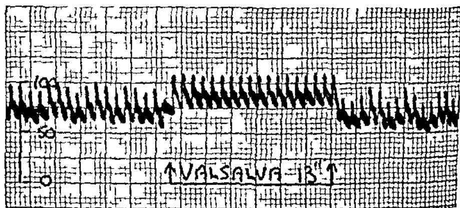


Fig 13 12—Valsalva manœuvre in a case of Pick s disease showing a square wave response in the arterial pressure pulse

Clinical features

The patient may be of either sex and almost any age but is usually an adult between 20 and 50 A previous history of tuberculous pericarditis or peritonitis is unusual

The onset of symptoms is insidious and signs may be well developed when the patient complains of little beyond fatigue slight breathlessness on effort fullness of the abdomen and perhaps a tendency to œdema Obvious ascites and dropsy are late symptoms although they may be the first that make the patient seek medical advice Cases with active tuberculous pericarditis of course are in a different category

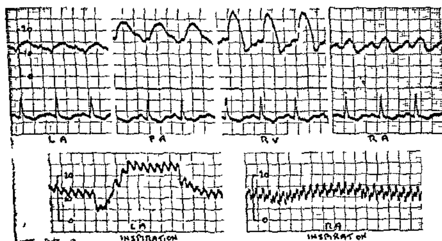
On examination the pulse is rather small and sometimes paradoxical almost disappearing with inspiration This is due to interference with cardiac filling when the pericardial tension is increased by descent of the diaphragm although it is the forward counterpart of Kussmaul s sign (*vide infra*) it is far less common The blood pressure is usually low The venous pressure is high and may rise appreciably during inspiration (Kussmaul 1873) A similar inspiratory rise of left atrial and pulmonary venous pressures may be recorded with the wedged catheter technique (fig 13 13) The chief wave in the venous pulse (fig 13 10) is usually the y trough (Friedreich s sign 1864) but in relatively mild cases with normal rhythm the *x* descent may be equally conspicuous Atrial fibrillation occurs in about one third of all cases its frequency is directly proportional to the age of the patient as in mitral stenosis and thyrotoxicosis

On palpation the heart is usually quiet, the left ventricular impulse

being barely perceptible and there being no lift over the right ventricle There may be an appreciable diastolic shock as if the heart filling rapidly under the influence of a high venous pressure suddenly met the unyielding resistance of a rigid pericardium which from a state of relaxation was thrown abruptly into tension on auscultation this is represented by an



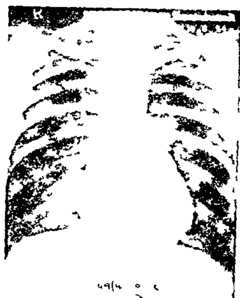
(a) Normal response the pressure falling during inspiration and rising during expiration



(b) Paradoxical response in a case of Pick s disease an even greater rise of pressure is seen in the left atrial pressure tracing

FIG 13 13—Effect of respiration on the left and right atrial pressure

accentuated and early third heart sound (Evans and Jackson 1952) Friction is absent Splitting of the second heart sound may fail to widen on inspiration for increasing the filling pressure of the right ventricle may not augment the stroke volume as previously explained In a minority of cases however not excluding those with the heaviest calcification not only does inspiration delay pulmonary valve closure as in normal individuals but



(a) Anterior view



(b) Calcification seen in second oblique view

Fig 13 14—Skiagrams of a case of constrictive pericarditis

Fig 13 15—Electrocardiogram in a case of chronic constrictive pericarditis

may also increase the intensity of the first heart sound In such cases the Valsalva manœuvre may be expected to give a normal response

Considerable enlargement of the liver ascites and œdema complete the clinical picture

Fluoroscopy reveals little cardiac pulsation, the heart shadow is normal in size in 45 per cent slightly enlarged in 17 per cent moderately enlarged in 32 per cent and greatly so in 6 per cent and has an ill defined outline (Paul Castleman and White 1948) Enlargement when present is due to the thickness of the pericardium which may measure as much as 26 mm (Freedman 1939) The shape of the heart shadow is also altered being triangular in half the cases with straight left and right borders and a small or absent aortic knuckle Calcification occurs in about half the cases and is best seen in the left anterior oblique position (fig 13 14)

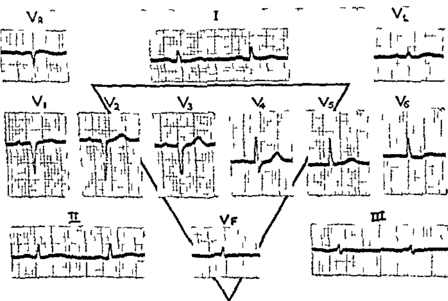


Fig 13 16—Almost normal electrocardiogram from a woman of 67 with Pick's disease (proved at operation)

The electrocardiogram usually shows low voltage QRS complexes with flattening or inversion of T in most leads representing the late stage of the pericardial T_2 pattern which in these cases is permanent (fig 13 15) A conspicuous or bifid P wave is not uncommon Occasionally the electrocardiogram is almost normal (fig 13 16)

Differential diagnosis It is insufficiently appreciated that the only pathognomonic sign of chronic constrictive pericarditis is a calcified pericardium and even this can occur without constriction Kussmaul's sign Friedreich's sign a loud and early third heart sound, and the characteristic electrocardiographic pattern can all occur in cases of isolated myocard

or other cardiopathy of clinically obscure origin A paradoxical pulse and the lack of much cardiac enlargement are highly suggestive of Pick's disease under the clinical circumstances but are not pathognomonic and are not necessarily present Poor ventricular pulsation on fluoroscopy is characteristic of most low output states

Because of these difficulties special efforts have been made to find some reliable physiological test that would distinguish Pick's disease without calcification from cardiopathies of clinically obscure nature but on the whole these efforts have failed and many fruitless thoracotomies have been undertaken in consequence This comment applies to intracardiac pressure pulses measurement of the cardiac output in relation to changes of posture and heart rate and the Valsalva manœuvre Unfortunately chronic constrictive pericarditis not infrequently behaves like heart failure and the tests themselves may give indeterminate results

Treatment Treatment consists of cardiac decompression achieved by surgical removal of the constricting tissue (Churchill 1929 1936) It has been assumed that the left side of the heart should be freed first to avoid the theoretical risk of acute pulmonary œdema but evidence is accumulating which suggests that constricting forces tend to be distributed equally over both ventricles and that division of constricting bands in any situation may result in generalised diminution of pericardial tension Removal of calcium may be difficult and time consuming but is amply rewarded The chief dangers during the operation are hæmorrhage and cardiac arrest or ventricular fibrillation The post operative course has been smoother since the advent of antibiotics for pulmonary and pleural sepsis can now be avoided or treated effectively The frequency of positive cultures obtained from pericardial tissue removed at operation has proved that activity is no direct bar to surgical treatment but has encouraged the concomitant use of streptomycin Even in subacute cases of tuberculous pericarditis of only six to twelve months duration, pericardiectomy should not be withheld on the grounds of florid activity if mechanical interference with forward flow is endangering life (Andrews Pickering and Sellors 1948)

The results of surgical treatment were good in 62 per cent of 415 cases reviewed by Chambliss *et al* (1951) and may be expected to be so in about three quarters of clinically inactive cases The surgical mortality over the last ten years has fallen from 33 per cent (Sellors 1946) to about 15 per cent (Chambliss *et al* 1951 Evans and Jackson 1952) The oldest patient operated on (successfully) in my own series was 67 years of age

Follow up studies in successfully treated cases reveal improved cardiac filling and forward flow reduction of left and right atrial pressures and disappearance of fatigue dyspnœa ascites and œdema but the physiology of the circulation is still abnormal venous pressures are higher than they should be, Kussmaul's sign may remain the third heart sound may still be heard although it may be softer and appreciably later (Mounsey 1955) normal rhythm is rarely restored the electrocardiogram is usually un

changed and the X ray appearances are much the same although the amplitude of cardiac pulsation may be greater Re constriction presumably as a result of low grade activity has necessitated a second operation in roughly 5 to 10 per cent of surviving cases over a period of 10 to 15 years precise figures on this point are not yet available

ADHERENT PERICARDIUM

During the first quarter of this century adherent pericardium was still considered an important complication of pericarditis Extensive adhesions anchoring the heart to adjacent resistant structures were believed to add a heavy burden to ventricular systole The theory was coloured by the pathological observations of Cabot (1926) who recorded gross cardiac enlargement associated with rheumatic adherent pericarditis The clinical picture included Broadbent s sign (indrawing of the postero lateral aspect of the ribs during ventricular systole resulting from fixation of the visceral pericardium to the diaphragm) paradoxical pulse diastolic shock or rebound of the ribs fixation of the apex beat so that it failed to shift with change of posture similar fixation of the electrical axis of the heart and unexplained cardiac enlargement To cure this unhappy condition the operation of cardiolysis (Brauer 1903) was devised to free the heart of its encumbrances by dividing adhesions between it and the surrounding tissues and especially by extensive rib resection so that the heart could pull against less resistant structures In more recent years, however, the serious consequences of adherent pericardium have been denied, and its surgical treatment is no longer favoured

Hosler and Williams (1936) failed to produce any cardiac enlargement or alteration of cardiac function by suturing the heart and pericardium to the diaphragm in 13 dogs nor could they find a single instance of cardiac enlargement in 76 cases of adherent pericarditis in which there was not an adequate organic intracardiac cause chiefly valvular disease Similar clinical and autopsy evidence was obtained by Armstrong (1940) in 72 cases and by Evans (Parkinson 1936) in 49 cases

All Cabot s cases of gross cardiac enlargement with adherent pericardium were complicated by serious valve disease Although Broadbent s sign (if not confused with indrawing of the left antero lateral aspect of the thorax which may occur whenever the heart is grossly enlarged) and diastolic rebound of the ribs are reliable signs of extrapericardial adhesions paradoxical pulse favours constriction and fixation of the apex beat or of the electrical axis is too variable to be of diagnostic value (France 1938)

TYPES OF PERICARDITIS BASED ON ETIOLOGY

Rheumatic pericarditis The dry form may give rise to nothing more serious than transient pericardial friction but it has an important bearing on diagnosis its advent during the course of rheumatic fever proving

beyond question the presence of active carditis More extensive pericarditis is usually associated with gross rheumatic infection so that serious carditis may be assumed These patients are often very ill, with high fever considerable dyspnœa or hyperpnœa, and much pain The development of cardiac dilatation and failure under similar circumstances is apt to be mistaken for pericardial effusion with cardiac compression and indeed the differential diagnosis may not be easy The position of the apex beat the ease with which it can be felt and the presence or absence of dullness in the second left intercostal space are good guides but the electrocardiogram may be indeterminate and the interpretation of skiagrams difficult (see page 488) Occasionally special diagnostic techniques may be necessary The safest of these is right atrial catheterisation (page 663) Angiocardiography is equally conclusive but less safe in these very sick children The results of paracentesis should be interpreted with more caution fluid may be obtained when there is a trivial amount present and failure to obtain fluid may be due to technical fault

Rheumatic pericardial effusion is a clear straw coloured sterile exudate it rarely compresses the heart tends to be resorbed spontaneously without undue delay appears to respond to salicylates and is usually best left alone

Fortunately there are no significant after effects for chronic constrictive pericarditis is never rheumatic and adherent pericardium though not uncommon is of little importance Pericardial calcification is seen occasionally but is scanty and harmless

Treatment is limited to relief of pain when present and to cardiac decompression in rare cases of high pressure effusion For the former antiphlogistine is comforting but when the pain is severe morphine should be given For the latter paracentesis is required and should be repeated when necessary Salicylates may also help Otherwise treatment should be directed towards the rheumatic illness as a whole

Tuberculous pericarditis Tuberculous pericarditis is uncommon in Great Britain it affects all age groups but favours coloured races and the male sex The infection usually spreads from mediastinal lymph gland or pleura (Peel 1948) Effusion is the rule and if the patient survives constriction may follow The onset is insidious and in cases with effusion a large quantity of fluid may collect before symptoms are noticed Dyspnœa and an irritable dry cough due to pressure on the lungs and bronchi are the usual complaints The absence of constitutional disturbances is often remarkable but continued fever anorexia loss of weight night sweats and secondary anæmia may occur in the more active cases Diagnosis depends upon the absence of rheumatic manifestations the subacute or chronic course of the malady the discovery of tuberculosis elsewhere and the results of culture and guinea pig inoculation of specimens of fluid obtained by paracentesis The effusion is usually a clear straw coloured exudate containing lymphocytes but is sometimes blood stained Occasionally the effusion is encapsulated and resembles a pericardial cyst radio-

logically (Freedman 1937) a tuberculous pericardial abscess presents a similar appearance The course is prolonged usually ranging between three and eighteen months and is often downhill with progressive emaciation toxæmia and anæmia cardiac compression may become dangerous, when frequent tapping adds to the patient s misery

It is doubtful if more than 20 per cent of untreated cases with positive cultures survive and of these the majority develop chronic constrictive pericarditis subsequently not infrequently active and constrictive stages are telescoped The prognosis is very different when tubercle bacilli cannot be recovered from the pericardial fluid the mortality rate being then less than 10 per cent (Harvey and Whitehill 1937) but of course the etiological diagnosis in many of these cases is open to question and very few constrict later Out of 71 untreated cases of tuberculous pericarditis reported by Carroll (1951) 53 5 per cent died within two years

Treatment with streptomycin 1 G intramuscularly daily or 2 G every third day in conjunction with para aminosalicylic acid (PAS) or its sodium alt 5–10 G twice daily by mouth or with isoniazid 100 mg twice daily by mouth for four to six months has reduced the mortality from at least 50 per cent to 15 per cent in proved cases (Goyette Overholt and Rapaport 1954) The immediate results of such treatment are good in 70 per cent of cases but it is too soon to assess the frequency of subsequent constriction It is already evident however that constriction is the rule if treatment is delayed more than four months from the recognised onset of the disease

Polyserositis Whilst tuberculosis may affect the pleura and peritoneum as well as the pericardium the term polyserositis (Concato s disea e) is usually reserved for a somewhat similar inflammatory process of unknown origin Large effusions collect in the serous sacs the fluid being a clear or opalescent straw coloured sterile exudate The process is obliterative and in the pleural cavity paracentesis must be performed ever higher as the two layers of pleura become fused together in a thick dense white matting Over the liver and spleen the greatly thickened peritoneum resembles a stout coating of sugar ice When the pericardium is involved resorption of fluid is followed by total obliteration of the pericardial cavity and con striction may ensue The course and prognosis are similar to those of tuberculous pericardial effusion

Benign (idiopathic) pericarditis Idiopathic pericarditis has been recog nised for at least a century (Christian 1951) The newer title *benign pericarditis* (Logan and Wendkos 1948) has the advantage of emphasising its most important feature

The M/F sex ratio is 3 1 The patient may be young middle aged or elderly with almost equal frequency the average age is 35 years About two thirds of reported cases have developed after an average latent period of twelve days following an upper respiratory tract infection (McGuire *et al* 1954) The onset is usually acute with fever malaise pericardial pain friction leucocytosis and raised sedimentation rate Effusion

develops in about two thirds of all cases but is rarely extensive The fluid is usually a straw coloured sterile exudate containing 3 to 4 G of protein per cent and a variable number of lymphocytes The electrocardiogram nearly always shows the typical changes of pericarditis

The course averages about six weeks with a range of two weeks to three months but nearly 20 per cent relapse occasionally several times the intervals between attacks varying between two and eight weeks This relapsing tendency is similar to that seen in traumatic and post operative pericarditis

Recovery is finally complete without calcification or constriction (Carmichael *et al* 1951) subsequent Pick s disease suggests that the initial diagnosis was wrong

In differential diagnosis benign pericarditis can usually be distinguished from cardiac infarction by the antecedent history of upper respiratory tract infection malaise and fever preceding pain the special characteristics of pericardial pain an early extensive and persistent friction rub, the development of pericardial effusion and the absence of abnormal Q waves in the electrocardiogram

No treatment has so far proved effective, although most of the newer antibiotics have been tried

Malignant infiltration of the pericardium When a male over 40 years of age complains of recent cough and breathlessness of insidious onset and is found to have a large pericardial effusion a malignant or tuberculous etiology is probable If there is no fever and the fluid is blood stained the diagnostic scales tip sharply in favour of malignancy When the pericardium is extensively invaded hæmorrhagic effusion and cardiac tamponade are the rule but when it is infiltrated by a single small nodule the fluid is usually clear and straw coloured and the sac being more distensible tamponade is less frequent The condition is invariably fatal and death never long delayed Autopsy usually reveals a primary bronchial carcinoma

Pyogenic pericarditis Streptococcal pneumococcal and staphylococcal infection may each give rise to pericarditis Fever leucocytosis and toxæmia are more conspicuous than in other forms Effusion is common and usually purulent It is generally believed that recovery may be followed by constriction, but this is certainly unusual if it occurs at all Streptococcal pericarditis may complicate tonsillitis erysipelas broncho pneumonia or any other streptococcal infection It usually occurs during the acute stage of the illness and is then readily distinguished from rheumatic pericarditis but when there is an appreciable latent interval this distinction is not so easy Pneumococcal pericarditis is usually a complication of left basal pneumonia organisms gaining access to the pericardium by direct spread from the pleura Staphylococcal pericarditis may complicate myocardial abscess from staphylococcal septicæmia

The course and prognosis of pyogenic pericarditis have been radically altered by chemotherapy Penicillin is more effective than the sulphona

mides and should be given in divided doses of 1 mega unit daily for seven to ten days Surgical drainage is only necessary when there is frank suppuration With such treatment initial recovery is the rule but the ultimate outcome is uncertain The lower mortality rate may result in an increased incidence of chronic constrictive pericarditis on the other hand the prevention of frank suppuration may have the opposite effect The few cases so far followed up by the author have not constricted

Hæmopericardium and traumatic pericarditis Hæmorrhage into the pericardial sac may be caused by stab or gun shot wound by rupture of a syphilitic or dissecting aneurysm of the aorta or by perforation of a myocardial infarct or ventricular aneurysm Wounds of the heart are not necessarily fatal and if the patient survives the initial insult relief of cardiac tamponade and surgical repair may be life saving Rupture of the heart or aorta into the pericardium is always fatal but not necessarily immediately A patient with a perforated infarct, for example may live as long as ten days

Severe blows crush injuries or blast may cause myocardial bruising and pericardial ecchymoses Transient pericardial friction and characteristic electrocardiographic changes usually provide evidence of the lesion If there is no damage to the superficial coronary arteries complete recovery is the rule

An interesting form of traumatic pericarditis may be due to pericardial foreign body (usually a metallic fragment) or to a foreign body lying close to the pericardium In these cases recurrent attacks of pericarditis with clear sterile effusion may occur at any time up to four months after the original injury The interval between attacks is usually two to six weeks during which the patient seems perfectly well The attacks themselves which last about a week tend to be severe with fever rapid effusion cardiac tamponade and considerable pain and distress Of seven cases that I reported in 1945 however, none died If the foreign body is easily accessible it is best removed in a quiescent period if not it may be safer to leave it *in situ*

Post operative pericarditis may follow any direct operation on the heart including mitral valvotomy aortic valvotomy via the left ventricular route pulmonary valvotomy and infundibular resection Its frequency is about 10 per cent Pericardial pain and fever usually lasting about a week are the chief manifestations pericardial friction common enough during the first week or two may reappear and a small effusion may develop The first episode usually occurs during the third or fourth post operative week sometimes just after the patient has been discharged from hospital Attacks are apt to be recurrent with intervals of two to three weeks over a period of two or three months

The syndrome is sharply reminiscent of the recurrent pericarditis associated with pericardial foreign body described above and may well be traumatic in nature (Wood 1954)

Uræmic pericarditis Pericardial friction is not uncommonly heard in patients dying with uræmia Symptoms are rare effusion absent and electrocardiographic changes minimal At autopsy needle like crystals of urea may be found massed in the pericardium



Fig 13 17—Pericardial effusion of three years duration in a case of extreme essential hyper tension

Pericarditis secondary to myo cardial infarction Acute myo cardial infarction may give rise to a local (60 per cent) or general (15 per cent) pericardial re action, and perforation may lead to hæmopericardium Local pericarditis is limited to the sur face area of the infarct gives rise to no symptoms and does not interfere with the electrocard iographic pattern of the under lying lesion A fleeting friction rub may be heard if the infarct is anterior

General pericarditis is less common but more important, it may cause additional pain allows anterior friction to be associated with posterior infarction (Stewart and Turner 1938) influences the electrocardiographic pattern and may even give rise to effusion

Chronic idiopathic pericardial effusion Large pericardial effusions of unknown cause may remain virtually unchanged for years It seems more than a coincidence that in my own series of six such cases all had hyper tension two of them malignant The effusion was usually gross (fig 13 17) and had lasted for at least three or four years in four of them There was no fever pain leucocytosis or raised sedimentation rate indeed, the effusion was virtually silent in all of them and in the two cases of malignant hypertension seemed to have prevented serious dyspnœa and orthopnœa by limiting the inflow to the right ventricle In the case illustrated for instance the intrapericardial pressure was 9 cm of saline and the venous pressure was raised proportionally the patient was able to lie flat and could even be tilted head downwards without distress after paracentesis orthopnœa and paroxysmal cardiac dyspnœa developed within three or four days and had to be controlled by dehydration until the pericardial effusion reaccumulated

The fluid in these cases has always been clear and acellular but has contained at least 4 G of protein per cent

In cases with severe hypertension it may be best not to disturb the physiological situation unless the blood pressure can be well controlled In cases without serious hypertension however partial pericardiectomy should be advised if the effusion is gross and chronic Mr W C Cleland undertook this operation in one of my cases at the Brompton Hospital after

repeated tapping and dehydration had failed to prevent rapid reaccumulation of fluid (fig 13 05) The condition had been present for at least four years and possibly for ten years The pericardium itself looked normal enough and there has been no trouble since

Chronic effusive pericarditis may also occur in children a good example in which the effusion was observed over a period of four years was reported by Contro *et al* (1955) in a child of 7 to 11

Hydropericardium Hydropericardium associated with congestive failure is rarely conspicuous and is of little clinical significance Pericardial effusion may also complicate myxœdema when it frequently contains cholesterol (Creech *et al* 1955)

Pericardial cyst A rounded opacity deforming the border of the heart shadow may represent a fibroma lipoma hydatid cyst cardiac aneurysm hæmatoma loculated pericardial effusion cold abscess or pericardial diverticulum or cyst

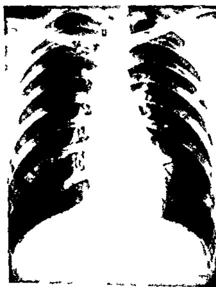


Fig 13 18—Pericardial cyst or diverticulum on the left border of the heart

Cardiac tumours usually alter the electrocardiogram and interfere with cardiac function hydatid disease can be recognised by Casoni and complement fixation tests cardiac aneurysm by paradoxical pulsation and characteristic electrocardiogram hæmatoma by the history of stab or gunshot wound and localised tuberculous abscess by subacute pericardial pain and local electrocardiographic changes A pericardial cyst or diverticulum, however is silent does not disturb the electrocardiogram and is discovered only on routine radiography (fig 13 18) It may be safely disregarded

Mediastinal tumours are more likely to be confused with aortic aneurysm and are therefore considered in the next chapter

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CHAPTER XIV

SYPHILITIC AORTITIS

SYPHILITIC inflammation of the aorta is clinically unrecognisable unless it results in fusiform dilatation saccular aneurysm aortic incompetence angina pectoris or possibly heart block It is true that many museums contain a specimen of syphilitic myocarditis and even of syphilitic endocarditis but these are oddities The various manifestations of syphilitic aortitis commonly appear from ten to thirty years after primary infection, usually between the ages of 30 and 60 account for about 3 per cent of all cases of organic heart disease in Britain and are approximately five times more common in men than in women Aortic incompetence is about twice as common as aneurysm

There can be little doubt that the disease is becoming less frequent and will become rare This is the result of educating the public in venereology and the improved treatment of early syphilis Thompson Comeau and White (1939) found cardiovascular syphilis had developed clinically in 10 per cent of 241 patients known to have had syphilis fifteen to twenty five years previously all had been inadequately treated by 1939 standards Uncomplicated aortitis rarely recognised except at necropsy is undoubtedly more frequent but its exact clinical incidence is difficult to assess published figures depending on the criteria upon which the diagnosis rests According to Moore only 16 per cent of 105 cases of uncomplicated syphilitic aortitis proved at necropsy were recognised clinically prior to 1932 (Moore *et al* 1932) whereas 68 per cent of 79 proved cases were correctly diagnosed in life between 1932 and 1941 (Mattman and Moore 1943) He ascribed this improved diagnosis to recognising the importance of a local substernal continual aching pain a tympanitic aortic second sound and slight dilatation of the ascending aorta in cases already known to have late syphilis It is pointed out however that the interpretation of such signs in patients who are *not* known to have late syphilis is another matter and their true value can only be judged properly under such circumstances

Whilst the clinical features may be diagnostic of a syphilitic etiology the latter may be confirmed by a history of syphilis, signs of syphilis in other systems (particularly neurosyphilis) a positive Wassermann or Kahn reaction in the blood in about 85 per cent of cases a positive treponema pallidum immobilisation test (Nelson and Mayer 1949 Friedman and Olansky 1955) and a persistently raised erythrocyte sedimentation rate

Congenital syphilis does not cause aortitis (McCulloch 1930) although

spirochætes may be present in the aorta there is practically no tissue reaction

Pathology The initial lesion occurs in the adventitia and consists of syphilitic endarteritis of the vasa vasorum and of focal granulomatous tissue Although the inflammation spreads deeply into the media atrophy and necrosis of muscular and elastic fibres are partly due to ischæmia The damage is patchy and is repaired by fibrous tissue, the cross section of the aortic wall being correspondingly thinned at such points These medial scars are indicated on the inner surface of the vessel by depressions of the intima which presents a pock marked appearance Secondary atherosclerosis and extensive calcification are common

ANEURYSM

Sooner or later the diseased media may yield to the force of the blood pressure either generally or at its weakest point and a fusiform or saccular aneurysm results A fusiform aneurysm is little more than an exaggeration of the inevitable dilatation of a syphilitic aorta and has no greater consequences It is usually associated with aortic incompetence but may be seen radiologically when still uncomplicated (Rich and Webster, 1952) it then affords acceptable clinical evidence of relatively early syphilitic aortitis The diagnosis should be confirmed by a history of syphilis or by positive serological tests however for fusiform aneurysm may result from congenital hypoplasia of the ascending aorta or from non specific medial necrosis with or without dissection and slight dilatation of the aorta may be due to atherosclerosis and hypertension A ringing or amphoric second heart sound at the base of the heart may denote dilatation of the ascending aorta but does not indicate its cause Again a suspicious aortic second sound must be disregarded if the ascending aorta is seen to be normal in size and shape Irregularities in the calibre of the ascending aorta or aortic arch which may be clearly demonstrated by means of angiocardiography and calcification of the ascending aorta provide good evidence of syphilitic aortitis

The syphilitic aneurysm proper is saccular (fig 14 01) and may occur in any part of the thoracic aorta particularly in the arch Aneurysm of the abdominal aorta is relatively rare and is less frequently due to syphilis Thus Mills and Horton (1938) attributed only 8 8 per cent of 80 abdominal aneurysms to syphilis and Estes (1950) only 5 per cent of 102 cases on the other hand Scott (1944) stated that syphilis was the cause of 58 per cent of his 96 cases The selective influence of specialised clinics no doubt explains the discrepancy

The M/F sex ratio in cases of saccular aneurysm is 10 1 (White 1937) partly perhaps because the aorta tends to be subjected to greater physical stresses in men than in women It is significant that saccular aneurysm rarely develops when there is aortic incompetence occurring in little over 10 per cent of such cases (Welty 1939) and that symptoms due to pressure

from an aneurysm may be relieved by an artificial arterio venous shunt conditions which reduce the mean aortic pressure

ANEURYSM OF THE ASCENDING AORTA

Aneurysm of the ascending aorta may cause visible pulsation or a conspicuous pulsating tumour to the right or left of the sternum or in the suprasternal notch Symptoms may be absent or there may be sternal or costal pain from pressure erosion Pulsation may be expansile and may be accompanied by a systolic thrill On auscultation a loud systolic bruit is usually heard When invisible an anterior aneurysm may yet be detected by percussing a band of parasternal dullness More often it is first discovered radiologically (fig 14 01)



Fig 14 01—Saccular aneurysm of the ascending aorta



Fig 14 02—Angiocardiogram showing partial superior vena cava obstruction due to an aneurysm

(By courtesy of D F nc Ga dner)

Partial obstruction of the superior vena cava is a not uncommon complication and gives rise to a high venous pressure in the head and neck while the right atrial pressure remains normal The distended jugular veins continue to pulsate as long as the obstruction is incomplete but if the venous pressure is very high pulsation may only be detected when the patient stands up A visible collateral venous circulation does not necessarily develop presumably because the block is incomplete so that a fair blood flow is maintained under the high head of pressure Puffiness or

œdema of the head and upper extremeties may occur, but in one case of the author's œdema was confined to the legs in the erect posture This was proved not to be due to anæmia chronic nephritis bilateral phlebothrombosis Milroy's disease low blood proteins thiamine deficiency or heart failure According to Katz (1954) chronic obstruction of the superior vena cava may result in salt and water retention by the kidneys in animals the mechanism is unknown The diagnosis of partial S V C obstruction may be proved by means of angiocardiography (fig 14 02) or by passing a venous catheter and noting the sudden fall in pressure as the tip slips through the obstruction

Aneurysm of the ascending aorta may rupture into the pericardial or pleural cavities into the pulmonary artery or into the right atrium

ANEURYSM OF THE ARCH

The symptoms and signs of an aneurysm in this situation are determined by pressure on surrounding structures Practically any structure in or close to the superior mediastinum may be compressed according to the size and position of the aneurysm Thus pressure on one or other subclavian artery may lead to significant differences in the pulse and blood pressure in the two arms a rare complication of this is clubbing of the fingers on the affected side Pressure on the left bronchus causes collapse of the left lung which may be complete or partial the upper lobe being involved more often than the lower Inflammatory changes may occur distal to the obstruction particularly bronchiectasis The left bronchus may be depressed with each pulsation of the aneurysm the resulting downward pull on the trachea during systole may be readily detected at the cricoid cartilage and is known as a tracheal tug It is best elicited by standing behind the patient who should be seated and applying steady upward pressure on the cricoid cartilage with the tip of one forefinger Pressure on the trachea itself may give rise to an irritating cough to stridor or to considerable respiratory obstruction pressure on the left recurrent laryngeal nerve to a brassy cough and paralysis of the left vocal chord pressure on the œsophagus to dysphagia The phrenic nerve usually escapes as it lies superficially but the left sympathetic chain may be compressed with the production of Horner's syndrome (homolateral contraction of the pupil and drooping of the upper eyelid) Severe radiating pains may be caused by pressure on nerve roots and the spine may be eroded

ANEURYSM OF THE ABDOMINAL AORTA

Of 1 459 aneurysms of the aorta collected from the literature by Unger and Poppel (1936) only 136 or less than 10 per cent were below the diaphragm and, as previously stated only about one in ten of abdominal aneurysms are syphilitic

An abdominal aneurysm usually presents as a pulsating tumour in the epigastrium over which a systolic thrill and murmur may sometimes be





(a) Anterior view (b) Second oblique position

Fig 14 03—Skiagram showing several aneurysms of the aortic arch

(By courtesy of Dr J h Parkinson)





(a) Anterior view (b) Lateral view

Fig 14 04—Calcified aneurysm of the aorta

detected Root pain associated with vertebral erosion is not uncommon or pain may be local A relatively common clinical error is to mistake a normal aorta projected forwards by lordosis in thin subjects for an aneurysm.

RADIOLOGICAL DIAGNOSIS



Fig 14 05 —Skiagram showing erosion of the bodies of several dorsal vertebræ as the result of pressure from an aneurysm

Although the existence and site of a syphilitic aneurysm may often be recognised clinically their accurate diagnosis is essentially radiological Aneurysm may be distinguished from other rounded shadows in the vicinity of the aorta by four characteristic features (1) it is intimately connected with the aorta (fig 14 03) (2) it becomes opaque with the aorta in angiocardiograms (3) it pulsates unless it is thrombosed (4) some part of its wall may be calcified (fig 14 04) Erosion of the bodies of several vertebræ (fig 14 05) and compression of the trachea bronchus or œsophagus may sometimes be seen Confusion may arise however when a mediastinal tumour exhibits transmitted pulsation Tomography and if necessary angiocardiography are advised in all doubtful cases

DIFFERENTIAL DIAGNOSIS

The chief problem is to distinguish aortic aneurysm from other space filling lesions in the mediastinum these include dermoid cyst lymphatic cyst thymic tumour intrathoracic goitre bronchial carcinoma and cold abscess of the spine In the author s experience all these have caused confusion whereas mediastinal adenopathy has not

Dermoid cysts are solitary anterior and present to one or other side of the mid-line they are rounded homogenous and sometimes calcified (fig 14 06) Solid teratomata are often irregular in outline and density and may contain teeth or bone

Lymphatic cysts are more posterior and may be single or multiple geographically they may be closely related to either the ascending or

descending aorta In the anterior skiagram they usually project either to the right of the ascending aorta or to the left in the region of the pulmonary artery or left atrial appendix (fig 14 07) In the latter position they may compress the pulmonary artery and cause physiological stenosis with all



Fig 14 06—Calcified d rmo d cyst proved at post mortem
(By cou tesy J S J h Park)



Fig 14 07—Lymphatic cysts (proved by re section)

the characteristic physical signs and catheter findings In the case illus trated in figure 14 08, for instance in which there was a typical pulmonary systolic thrill and murmur the right ventricular pressure was 70/3 mm Hg and the pulmonary artery pressure beyond the point of compression 18/12 mm Hg when the cardiac output was 8 L/min

Thymic tumours or cysts are also anterior and often malignant I have seen two calcified thymic cysts of many years duration both of which finally became malignant and invaded the pericardium and myocardium In anterior skiagrams the cyst or tumour presented to the left of the mid line just below the aortic knuckle (fig 14 09a) and in lateral views was seen to be well anterior (fig 14 09b) Pericardial pain effusion atrial flutter or fibrillation and characteristic electrocardiographic changes developed in both instances

Retrosternal goitre is easily recognised if it moves upwards on swallowing but may be mistaken for aneurysm if malignant and fixed

Bronchial carcinoma with secondary invasion of mediastinal glands and partial obstruction of the superior vena cava may sometimes be mistaken for aneurysm

Tuberculous cold abscess secondary to Pott s disease of the dorsal spi



(a) Anterior view



(b) Angiocardiogram of pulmonary artery



(c) Angiocardiogram of aorta



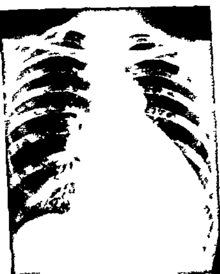
(d) The cyst after removal

Fig 14 08—Lymphatic cyst compressing the pulmonary artery

may sometimes be identified by its irregular ramifications especially when old and calcified In its active stage however it may present as a fusiform swelling behind the heart and may be mistaken for a syphylitic or dissecting aneurysm of the descending aorta

Tomography and *angiocardiography* have proved of great value in distinguishing aortic aneurysm from these and other mediastinal masses

Retrograde aortography is rarely necessary and in cases of syphilitic aortitis is probably dangerous



(a) Anterior view enlargement of the heart shadow is due to pericardial effusion



(b) Second oblique view showing the anterior superior position of the tumour

Fig 14 09—Calcified cystic malignant tumour of the thymus invading the pericardium and myocardium

The differential diagnosis between syphilitic and other forms of fusiform dilatation of the aorta is considered later in relation to aortic incompetence

COURSE

Many aneurysms remain silent and are discovered accidentally by radiography others cause much suffering One of the worst features is the severe pain produced by pressure on bone especially the root pain associated with vertebral erosion This may last for months and be very resistant to treatment

The prognosis varies greatly but the average duration of life is little more than eighteen months from the onset of symptoms (Colt 1926–27) Cases have been reported however which have survived for fifteen to thirty years (Kauntze 1947) The chief dangers are infection of the lungs distal to bronchial compression and rupture Aortic aneurysm may rup

ture into the pericardium the pulmonary artery, the trachea or bronchus the œsophagus or the pleura giving rise to hæmopericardium with cardiac compression acute right ventricular failure with signs and symptoms of an aorto pulmonary shunt, dramatic hæmoptysis hæmatemesis or hæmothorax respectively usually with fatal results

SPECIAL TREATMENT

The object of treatment apart from anti syphilitic measures is *to promote thrombosis and calcification in the aneurysmal sac or to protect it by means of external fibrosis in order to prevent rupture or further expansion*

Bed rest is necessary at first while routine anti syphilitic treatment is given During this period a course of calcium lactate 10 grains (0 6 G) t d s with vitamin D may be added to promote calcification in the wall of the aneurysm

If pain is not relieved by these measures surgical interference may be considered The old operation of inserting a wire into the sac in order to induce thrombosis is unsatisfactory the risk is considerable and effective clotting cannot be guaranteed Babcock s operation—the creation of an arterio venous communication between the carotid and jugular vessels (Babcock 1926 1932)—reduces the mean aortic pressure and may relieve pain (Ranson 1947) A more promising surgical method is to wrap the aneurysm in polythene cellophane this causes an intense fibroblastic reaction which protects the sac from without prevents further expansion and relieves pain (Poppe 1948) Resection of the aneurysm and replacement by an aortic homograft may be feasible when the lesion is below the left subclavian artery (Debakey and Cooley 1953 Rob 1954)

AORTIC INCOMPETENCE

Pathology Weakening of the mesaorta in the region of the aortic valve leads to dilatation of the aortic ring and to separation of the cusps at their commissures so that the valve becomes incompetent Granulomatous tissue may also drive a wedge between the junctions of the cusps (fig 14 10) The cusps themselves become rolled and thickened at their free margins and present a dwarfed stunted appearance There is no stenosis and calcification is absent unless there is much secondary atherosclerosis Owing to the site of the lesion which is necessarily at the root of the aorta the mouths of the coronary vessels are often partly occluded either by active granulation tissue or fibrotic scarring Ischæmic fibrosis of the myocardium results

Incidence Syphilis used to account for about one third of all cases of aortic valve disease and for about one half of those in subjects between the ages of 40 and 60 (Cowan and Ritchie 1935) Of Campbell s series of 300 cases of aortic valve disease syphilis was responsible for 19 per cent only half of his cases however had aortic incompetence alone and of these syphilis was the cause in 38 per cent (Campbell 1932) At the present time

syphilis is probably still the most common cause of pure aortic incompetence between the ages of 40 and 60 but its frequency is declining

The sex ratio in syphilitic aortic incompetenc is about 3 1 in favour of men (Campbell 1932) and is thus less remarkable than in aneurysm



Fig 14 10—Act e syphilitic aortitis in a man of 6 showing granulomatous thickening around the coronary orifices and between the commissures of the thickened aortic cusp

Clinical features Syphilitic aortic incompetence has all the features of aortic incompetence in general (page 564) and some special characteristics of its own Only the latter will be considered here

1 The history of symptoms or of the discovery of the lesion is relatively recent usually a matter of weeks or months and rarely more than a year or two

ture into the pericardium the pulmonary artery, the trachea or bronchus the œsophagus or the pleura giving rise to hæmopericardium with cardiac compression acute right ventricular failure with signs and symptoms of an aorto pulmonary shunt dramatic hæmoptysis hæmatemesis or hæmo thorax respectively usually with fatal results

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AORTIC INCOMPETENCE

Pathology Weakening of the mesaorta in the region of the aortic valve leads to dilatation of the aortic ring and to separation of the cusps at their commissures so that the valve becomes incompetent Granulomatous tissue may also drive a wedge between the junctions of the cusps (fig 14 10) The cusps themselves become rolled and thickened at their free margins and present a dwarfed stunted appearance There is no stenosis and calcification is absent unless there is much secondary atherosclerosis Owing to the site of the lesion which is necessarily at the root of the aorta, the mouths of the coronary vessels are often partly occluded either by active granulation tissue or fibrotic scarring Ischæmic fibrosis of the myocardium results

Incidence Syphilis used to account for about one third of all cases of aortic valve disease and for about one half of those in subjects between the ages of 40 and 60 (Cowan and Ritchie 1935) Of Campbell's series of 300 cases of aortic valve disease syphilis was responsible for 19 per cent only half of his cases, however had aortic incompetence alone and of these syphilis was the cause in 38 per cent (Campbell 1932) At the present time

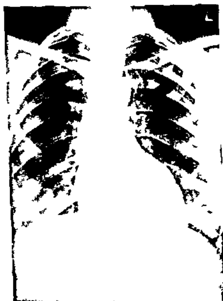


Fig 14 12—Syph lit c aortic incompetence the appearances here differ little from other forms of aortic valve disease



(a) Anterior view



(b) Second oblique position

Fig 14 13—Calcification of the ascending aorta in a case of syphilitic aortitis

(By ourt sy f Dr J S M C nn d Dr D C Porter)

there is no stenosis no valve calcification no mitral valve disease and no rheumatic history Most syphilitic cases under the age of 30 are at first mistaken for rheumatic aortic incompetence especially because in these active granulomatous cases there is little if any dilatation of the ascending aorta or no more so than in any other type of free aortic incompetence A rheumatic etiology is favoured if the lesion is known to have been present for many years if there is no angina pectoris and if the sedimentation rate is normal

Old dissecting aneurysm of the ascending aorta involving the aortic valve and causing free incompetence is frequently mistaken for syphilitic aortitis even a fresh dissection with rapidly developing aortic incompetence may be confused with syphilis the new and severe valve lesion then being attributed to a ruptured cusp The dilated appearance of the ascending aorta and the free regurgitation lend credence to the error Occlusion of one or more of the great vessels arising from the arch of the aorta does not distinguish dissecting aneurysm from syphilitic aortitis—indeed the latter is the commonest cause of what has been termed reversed coarctation meaning normal femoral pulses and diminished or absent pulses in the subclavians and carotids This syndrome, also known as pulseless disease or Takayasu's disease is sometimes caused by a primary arteritis of the aortic arch especially when it occurs in young women (Ross and McKusick 1953) but in such case there is no aortic incompetence

Old dissecting aneurysm (q v) should be suggested by the history the presence of hypertension the negative serology and the normal sedimentation rate

Congenital hypoplasia of the ascending aorta (q v) may cause conspicuous dilatation of the aorta from the valve ring to the origin of the innominate artery with free aortic incompetence Associated arachnodactyly some other congenital anomaly or the long history may at once suggest the correct diagnosis

Bacterial aortic endocarditis active or old is sometimes confused with syphilitic aortitis Aneurysm of an aortic sinus perforation of a cusp free aortic incompetence high sedimentation rate and the development of severe heart failure towards the end of penicillin treatment are common to both diseases If the fever is low grade blood culture negative and W R doubtful the differential diagnosis may be very difficult in the absence of other pathognomic signs of bacterial endocarditis

Atherosclerotic aortic incompetence is suggested by the age of the patient some evidence of stenosis calcium in the aortic knuckle but not in the ascending aorta, and valve calcification Angina pectoris is common owing to the frequency of associated coronary disease but the sedimentation rate is normal and serology negative

Course The prognosis is bad the average duration of life being about two years (Campbell 1932) Left ventricular failure develops sooner or later in many cases, and congestive heart failure follows The downhill

course differs from that of other forms of aortic incompetence in its rapidity in the frequency of angina pectoris and in the relatively high proportion of sudden deaths (Munck 1946)

A rather more hopeful outlook is given by Webster *et al* (1953) who were able to trace 75 per cent of 1 020 cases seen over a period of twenty years at the Johns Hopkins Hospital 51 per cent of those that were initially sympton free survived ten years when angina pectoris was present 28 per cent survived ten years, when congestive failure was present only 6 per cent so survived

ANGINA PECTORIS

Pathology It is often said that aortic valve disease may cause angina pectoris Whilst this is true the statement needs amplification Angina is a common complication of all forms of aortic stenosis and of syphilitic aortic incompetence but not of other varieties Rheumatic aortic incompetence for example must be gross to cause angina and rarely does so The explanation is to be found in the physiology of the coronary circulation During systole ventricular contraction prevents blood flowing through coronary vessels which penetrate left ventricular muscle and large arteries on the surface dilate to form an elastic reservoir which in recoil during diastole acts as an accessory pump forcing the blood onwards The higher the systolic pressure the greater the elastic reservoir provided the coronary arteries are healthy During ventricular relaxation blood is able to flow through vessels penetrating muscle being propelled by the aortic diastolic pressure and by the recoil of the elastic reservoir just mentioned Thus the coronary flow depends upon both systolic and diastolic pressures i e upon the mean pressure

Now in aortic stenosis the mean blood pressure is often low but in aortic incompetence although the diastolic pressure may be 40 or 50 mm of mercury the systolic pressure is commonly raised and the mean pressure adequate Syphilitic aortic incompetence causes angina pectoris because there is associated stenosis of the mouths of the coronary arteries if syphilitic aortitis produces sufficient damage in the region of the aortic cusps to cause aortic incompetence it is unusual for the mouths of the coronary vessels to remain unscathed Conversely if the mouths of the coronary vessels are so stenosed as to cause angina pectoris it is practically impossible for the root of the aorta to remain healthy Thus syphilitic angina is rare without aortic incompetence

Clinical features Syphilitic angina has certain characteristics which help to distinguish it from other types (1) the attacks tend to be of longer duration (2) they are more often nocturnal although the ordinary relationship to effort holds good (3) they are less often relieved by trinitrin Coronary thrombosis is a rare complication because ischæmia is due to stenosis of the coronary ostia and not to changes in the coronary vessels themselves Myocardial infarction however may occur without coronary thrombosis,

especially when the effect of gross occlusion of the mouths of the coronary vessels is exaggerated by a drop in blood pressure from some other cause, such as surgical shock. Ischæmia of the least nourished part of the myocardium may then be so pronounced as to cause necrosis, even so cardiac infarction is uncommon. Of 58 cases of sudden death from syphilitic aortitis studied by Munck (1946), for instance, only four had a myocardial infarct.

Course. The prognosis is poor; 75 per cent of patients living less than ten years (Webster *et al.* 1953). Status anginosus may develop before the end, or nocturnal angina may prove troublesome. When heart-failure develops angina may disappear; it is not clear why this should be so, but it may depend upon changes in tissue metabolism.

Special treatment. The ordinary methods of treating angina pectoris are applicable to the syphilitic type, although the results are poor. Anti-syphilitic measures should not be withheld. Bed rest is particularly important during the first six weeks of treatment, and is essential during the first course of penicillin (or arsenic). In relatively young subjects with granulomatous obstruction of the coronary ostia, remarkably good results may be achieved with penicillin.

HEART BLOCK

True syphilitic heart block is very rare, and depends upon interruption of the bundle of His by gummatous tissue. On the other hand, heart block resulting from interference with the conducting tissue by ischæmic fibrosis due to stenosis of the coronary ostia is not uncommon, and like angina pectoris, and for the same reason, is nearly always associated with aortic incompetence. The former may respond to iodine or penicillin therapy, the latter, of course, does not.

SPECIFIC TREATMENT OF SYPHILITIC AORTITIS

Syphilitic aortitis should be fully treated with anti-syphilitic drugs, whether uncomplicated or otherwise. Clearly past damage cannot be repaired, but active granulomatous tissue can be abolished and further activity prevented.

The patient should be put to bed for four weeks, and during the first three weeks should receive potassium iodide 10 grains (0.6 G.) t.d.s., preferably with liq. hydrarg. perchlor. 60 minims (4 ml.). Gummatous tissue resolves with this treatment, and the danger of a severe Herxheimer reaction is lessened. After two to three weeks of such treatment 1.2 million units of procaine penicillin are given over a period of 10 days in divided doses of 600 000 units twice daily. Alternatively a single daily injection of 600 000 units of penicillin may be given over a period of three weeks. Reactions are rare (Moore 1947).

Shortly after completing the penicillin course the patient may be allowed up and treatment with bismuth begun. Intramuscular injections of 0.1 G.

of bimostab weekly for six weeks followed by 0 2 G weekly for the next six weeks are advised Some prefer to start treatment with bismuth and dispense with iodine and mercury altogether Others use penicillin alone In view of its more toxic nature arsenic has now been abandoned in the treatment of cardiovascular syphilis being superseded by penicillin

The development or aggravation of angina pectoris or heart failure are major dangers but both are unlikely and when they do occur cannot always be attributed to the treatment

Herxheimer reactions are not prevented by starting with small doses of penicillin but are inhibited by preliminary iodine mercury or bismuth The occasional development of heart failure following penicillin treatment is attributed to an increase in the degree of aortic incompetence as contracting scar tissue replaces granulomatous inflammation A rather similar situation is common in bacterial endocarditis

The regime described constitutes one complete course of treatment and lasts four months The situation should then be reviewed particular attention being paid to the E S R If this is normal treatment may be discontinued but if still raised, a second course of penicillin is advised Bed rest is no longer necessary unless congestive failure, angina pectoris or some other complication demands it Since there is now no danger of a Herxheimer reaction there is no need to repeat iodine mercury or bismuth

A third or fourth course of penicillin should be given without hesitation if there is any further evidence of activity

It is repeated for emphasis that neither aneurysm angina pectoris nor heart failure contraindicates penicillin for the Herxheimer reaction is rare This phenomenon consists of a local tissue reaction which may cause swelling and occlusion of the coronary ostia with disastrous results

Statistics have shown that the effect of full anti syphilitic measures before the introduction of penicillin was to improve the average life expectancy from eighteen months to two years (Padget and Moore 1935) It may be argued that the increased care and enforced rest which are a necessary corollary to this form of treatment might also improve the prognosis by a similar amount and there is something to be said for the view that there is little point in attempting to extirpate the spirochæte once heart failure or angina pectoris has developed for it is then probably too late However the great majority of untreated cases show active syphilitic aortitis at necropsy whereas treated cases do not (Webster and Reader 1948) and there are a sufficient number of cases that benefit from subsidence of this active inflammation to make routine treatment well worth while

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CHAPTER XV

ISCHÆMIC HEART DISEASE

DEFINITION

OCCLUSIVE disease of the coronary arteries of sufficient degree to prevent the coronary circulation meeting the physiological demands of the heart is best described as ischæmic heart disease It is characterised clinically by angina pectoris acute coronary insufficiency, and cardiac infarction pathologically by occlusive coronary atherosclerosis with or without thrombosis, and by focal or massive ischæmic myocardial necrosis and fibrosis

INCIDENCE

Occlusive coronary atherosclerosis is responsible for about 30 per cent of all cases of organic heart disease and for about 80 per cent of all sudden *cardiac deaths (Munck 1946) moreover it appears to be increasing rapidly* thus the number of cases dying from coronary disease in England per million persons living was 48 in 1926, 148 in 1930, 473 in 1939 (Cassidy *1946) and 1 392 in 1953 (Registrar General s review)* The increasing age of the population is no doubt partly responsible thus the citizens of ancient Rome in their halcyon days had an average life span of twenty to thirty years and the following table shows the increased average life span in the U S A from 1879 to 1944 (Master 1947)

1879–1899	34 years
1911–1912	46 63 years
1919–1920	51 14 years
1930	57 36 years
1944	64 40 years

These remarkable figures are chiefly due to the successful war against *infections and parasitic diseases and to the saving of life by surgical means* Another factor that must be taken into account is the attitude of medical practitioners who in 19_6 had scarcely heard of coronary thrombosis whereas now they are apt to *diagnose it more frequently than it exists It* should be remembered that coronary thrombosis was not recognised as a clinical entity until its classic description by Herrick in 1912 despite Leyden s lucid account in 1884 and was not *widely appreciated in Great* Britain until popularised by McNee in 1925 and Gibson (1925)

Sex Of Heberden s 100 cases of angina only three were women (Heberden 1802) Most investigators give the general sex ratio as *4 1 in* favour of men but under the age of 50 it is 8 1 (Hedley 1939) and under the

age of 40 male predominance is overwhelming in fact, angina in women under 40 is nearly always due to some other etiological agent such as hypertension aortic stenosis syphilitic aortitis anæmia, myxœdema diabetes mellitus xanthomatosis or paroxysmal rhythm change Between the ages of 60 and 70, however about one third of the cases are women and over the age of 70 the sex incidence is equal (Gordon Bland and White 1939)

Age Of 1 000 cases seen personally by Cassidy (1946) 70 per cent were between 50 and 70 years of age of the men 14 6 per cent were between 40 and 50 3 2 per cent between 30 and 40, and 0 25 per cent were under 30 These figures are in harmony with common experience except perhaps with regard to the incidence in young men, for many such cases were seen in the Services during the second world war (Newman 1946 Poe 1947) The peak age of death is 60 (Hedley 1939)

Hereditary factor A familial incidence of coronary disease was found in 50 per cent of Cassidy's 1 000 cases and was four times as common in Yater's 744 young cases (under 40) as in normal controls (Cassidy, 1946 Yater *et al* 1948)

Habits and occupation There is a general impression that the incidence of ischæmic heart disease is particularly high amongst professional men and is related to the stress of modern urban life There is said to be little to support this view (Master 1947) but some figures published by Hedley (1939) are interesting

Occupation	*Deaths from coronary occlusion per 100,000*
Professional	154
Managers and officials	140
Clerks and salesmen	128
Skilled and unskilled workers	107

The author however ascribed the difference in these figures to more accurate certification in those earning larger incomes

Nevertheless the obstinate belief that angina pectoris is a doctor's disease persists and appears to be justified by startling figures published by Ryle and Russell (1949) These workers who were especially well qualified to sift and present evidence of the kind required divided the social strata of England and Wales into five classes and found that the standardized mortality ratio (S M R) from ischæmic heart disease in social class I (professional workers) was twice that in social class III (skilled artisans) and three times that in class V (unskilled workers) Their table giving the actual occupations with the four highest and four lowest standard mortality ratios ends the debate on this previously vexed question and once again emphasises the fact that experienced opinion should not be too readily cast aside because of ill founded statistical evidence to the contrary Physicians and surgeons head the list with an S M R of 368 proprietors of wholesale business came second with an S M R of 235 the legal profession third

(227) and the Church fourth (218) At the other extreme we have workers in chemical processes with an S M R of only 20 agricultural labourers 32 stone miners and quarriers 38 and coal miners engaged in other work 40 More recently Morris *et al* (1952) showed that ischæmic heart disease was twice as common in general practitioners as in consultants or specialists

It is by no means clear what factors are responsible for the higher incidence of ischæmic heart disease in certain occupations and social classes the degree of mental stress and strain or other psychological factor the type of diet or standard of nutrition and the amount of day to day physical inactivity have each been suspected but as yet there is little convincing evidence favouring one more than another Morris *et al* (1953) however have brought forward interesting data which they thought might implicate physical inactivity They found for instance that conductors on double decker buses and po tman were less likely to develop ischæmic heart disease than bus drivers executive officers telephonists and post office clerks

There is no evidence that alcohol (Wilens 1947) is responsible for the high male incidence or has any permanent influence on the course of the disease Cassidy (1946) exonerated smoking but recent statistical studies have shown that ischæmic heart disease is about one and a half times more common in cigarette smokers than in non smokers (Doll and Hill 1954 Hammond and Horn 1954)

PATHOGENESIS

Ischæmic heart disease is due to occlusive coronary atherosclerosis with or without secondary subintimal hæmorrhage or thrombosis Angina pectoris caused by *syphilitic aortitis* aortic stenosis severe anæmia paroxysmal tachycardia and the like and coronary occlusion resulting from angiitis *embolism* trauma dissecting aneurysm and other rarities are considered elsewhere

The cause of human atheroma remains unknown despite a great deal of work on the subject (Cowdry 1933 Katz and Stamler 1953) The word atheroma comes from the Greek αθηρη meaning groats i e crushed corn or gruel (American mush) and ωμα a swelling Lipoid substances accumulate in the intima of the aorta and larger arteries in a patchy irregular fashion causing a variable degree of pressure atrophy of the underlying media and sometimes *encroaching* on the lumen of the vessel (fig 15 01) The degree of narrowing of an atherosclerotic coronary artery cannot be accurately assessed by its appearance at necropsy, for in life the blood pressure tends to iron out the excrescences and maintain a smooth intimal surface and full lumen (*Harrison* and Wood 1949) Indeed Duguid and Robertson (1955) maintain that an atherosclerotic vessel *per se* is dilated and that narrowing of the lumen is only caused by thrombosis

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Hunter (1796) Erosion or ulceration of atheromatous lesions forms an excellent nidus for secondary thrombosis This is the common cause of acute coronary obstruction Organisation of such thrombi leads to micro copical appearances similar to atherosclerotic lesions indeed it has been

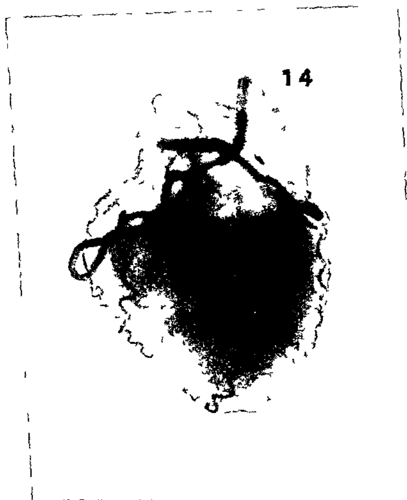


Fig 15 01 (b)—Normal control for comparison

suggested that atheroma may represent nothing more than intravascular clotting (Duguid, 1946 1948)

Etiology of atherosclerosis

As a result of a vast amount of work on this important subject the sterile doctrine that atherosclerosis is an inevitable consequence of growing old has been largely abandoned instead it is now believed that atherosclerosis

is closely related to disturbances of fat metabolism usually acting over a long period of time (Katz and Stamler 1953) and perhaps also to some alteration in the biophysical properties or biochemical structure of the intima itself (Page 1954) The evidence upon which these conclusions are based can be summarised only very briefly here, but before doing so it may be helpful to digress for a moment on the nature of the blood lipids

The blood lipids

Fatty substances in normal blood include neutral fat fatty acids free cholesterol cholesterol esters and phospholipids

Following a fatty meal the plasma may become opalescent this is due to the transport of neutral fat and fatty acids combined with protein in the physical form of chylomicrons which are microscopically visible fatty bodies less than 1μ in diameter Moreton s view that these bodies might play an etiological role in atherosclerosis (Moreton 1948) has not been shared by subsequent workers (Gofman *et al* 1950) Chylomicrons contain less than 5 per cent of cholesterol have very high S_f values around 40 000 units (*vide infra*) and change their structure after an injection of heparin when they develop S_f values under 10 (Graham *et al* 1951)

Cholesterol and phospholipids also of course insoluble in water are carried in combination with α and β globulins as α and β lipoproteins which are microscopically invisible macromolecules of various sizes and densities The total *serum cholesterol*, which is normally around 150 to 300 mg. per cent, is certainly related to atherosclerosis but has been found to be only a crude measure of blood lipid disturbance

Gertler *et al* (1950) emphasised the part played by the cholesterol esters and the *phospholipids* and suggested that the cholesterol/phospholipid ratio was more closely related to atherosclerosis than the total serum cholesterol This ratio is normally about 0 85 to 1 0 (Barr 1953) the amount of phospholipid tending to be proportional to the amount of free cholesterol present rather than to the quantity of cholesterol esters Ratios above unity mean that the cholesterol esters have risen more than the free cholesterol High ratios are found in all diseases known to encourage atherosclerosis

Such measurements however give no information about the biophysical properties of the macromolecules in which these substances are incorporated The lipoproteins however may be fractionated biochemically (Cohn *et al* 1946) or by means of electrophoresis (Pearsall and Chanutin 1949) or the ultracentrifuge (Gofman *et al* 1950) Russ Eder and Barr (1951) found that practically all the serum cholesterol was incorporated in Cohn s fractions A and C, i e in the α_1 and β_1 lipoproteins 30 per cent in the former and 70 per cent in the latter They also found that the cholesterol/phospholipid ratio was about 0 5 for the α_1 lipoproteins and 1 35 for the β_1 lipoproteins (If phospholipids are expressed in terms of phosphorus these ratios should be multiplied by 25) In atherosclerosis

and diseases known to encourage it, there is a relative and usually absolute increase in the β_1 lipoproteins even when the total blood cholesterol is normal and the cholesterol/phospholipid ratio less than unity (Barr, Russ and Eden 1951 Oliver and Boyd 1955)

In the hands of Gofman and his associates (1950) the ultracentrifuge proved a useful tool for separating lipoproteins of different densities The density of the macromolecules believed to be most closely related to atherosclerosis is close to 1 G /cc If the density of the solution containing them is adjusted to 1 063 by means of sodium chloride they will float with varying degrees of facility according to their densities The α_1 lipoproteins being denser than the solution will not float and are therefore immediately separated out In the Svedberg ultracentrifuge molecules that sediment at a rate of 5×10^{-13} cm per second per unit field of force are said to have a value of 5 S (Svedberg) units For flotation rates the same Svedberg unit is used with the suffix f Thus molecules that float at rates of 20×10^{-13} cm per second per unit field of force are said to have an S_f value of 20 It will be understood therefore that the higher the S_f value the lighter the molecule. Using this technique Gofman *et al* (1950) have divided the lipoproteins into classes according to their flotation rates. Those not analysed being denser than 1 063 (the arbitrary density of the solution) are the α_1 lipoproteins which do not seem to be closely correlated with atherosclerosis Of the large β_1 lipoprotein fraction the chief S_f classes are 2 to 10 12 to 20, 20 to 35 35 to 100, and 100 to 40 000 The lipoproteins shown to be closely related to atherogenesis are those with S_f values of 12 to 20 and 35 to 100 (Gofman *et al* 1952)

Evidence that atherosclerosis is related to altered blood lipids

The chief evidence supporting the view that atherosclerosis and ischæmic heart disease are related to disturbances of blood lipid transport or metabolism may now be summarised

1 In the animal kingdom man alone suffers commonly from atherosclerotic disease the total blood cholesterol cholesterol esters cholesterol/phospholipid ratio β_1 lipoproteins and the concentration of lipoprotein macromolecules of the S_f 10–20 and 35–100 class are all considerably higher in man than in any other mammal (Barr 1953)

2 Only the new born normal infant is immune from atherosclerosis children young adults and women during the child bearing age are relatively immune the frequency of atherosclerosis in men increases with age at least up to the end of the sixth decade The blood concentration of the particular classes of lipoprotein mentioned above is relatively low in the more or less immune groups but relatively high and increases with age in susceptible men (Gofman *et al* 1950)

3 Œstrogens tend to restore the normal blood lipid pattern (Barr 1953) androgens have the reverse effect (Russ *et al* 1955) Atherosclerosis increases after bilateral oophorectomy in women (Wuest Dry and

Edwards 1953) By the age of 70 the M/F sex ratio in ischæmic heart disease is unity

4 All diseases known to be associated with the altered blood lipid pattern described above are also associated with a high incidence of severe atherosclerosis these diseases include diabetes mellitus, myxœdema xanthomatosis nephrosis and familial hypercholesterolæmia (Gofman *et al* 1951 Katz and Stamler 1953) The same abnormal blood lipid pattern is the rule in spontaneous ischæmic heart disease

5 Atherosclerosis has been produced experimentally in animals only by means of a high cholesterol intake first in rabbits (Anitschkow, 1913 Leary 1934) then in chicks (Dauber and Katz 1942) dogs with the aid of thiouracil (Steiner Kendall and Bevans 1949) hamsters (Goldman and Pollack 1949) and guinea pigs (Altschul, 1950) Experimental atherosclerosis in omnivorous animals has the same distribution as in man

6 The atheromatous lesions themselves contain a high proportion of cholesterol (Windaus 1910) as has been known for a century (Cowdry 1933)

7 Atherosclerosis is rare in people who live on a vegetarian diet low in fat (Steiner 1946) and the incidence of clinical diseases due to atherosclerosis fell sharply in Northern Europe during the second world war parallel to the decline in the consumption of foods rich in cholesterol (Malmros 1950) According to Wilens (1947) severe atherosclerosis is ten times as common in obese subjects as in the lean Keys (1952) emphasized the importance of total fat intake rather than cholesterol intake per se Gofman and Jones (1952) have shown that obese subjects tend to have a higher concentration of lipoprotein of the S_f 35–100 class than lean subjects, there was less relationship however between obesity and lipoproteins of the S_f 12–20 class Gofman *et al* (1950 1951) have also shown that prolonged low fat diets gradually reduce the blood concentration of the abnormal lipids

The part played by the intima

While it is now generally agreed that abnormal blood lipids are an important factor in the production of atherosclerosis it is far from clear just how they operate

Wilens (1951) showed that serum could filter through an artery from the lumen outwards Experimentally the filtrate was unchanged serum in respect of most inorganic substances but contained very little cholesterol relatively little protein and a diminished amount of calcium these substances becoming highly concentrated in the serum within the vessel The rate of filtration was proportional to the filtration pressure i e to the blood pressure, Some of the cholesterol penetrated the intima but its further progress was barred by the internal elastic lamina

The filtration theory of atherogenesis (Page 1954) is based on observa-

tions of this kind and implies that cholesterol deposits may accumulate gradually over the years in normal individuals but that they may do so much more rapidly and in far greater degree in the presence of raised blood lipoproteins of the kind best adapted to penetrating the intima especially if the filtration pressure is high (as in hypertension) and if there are changes in the ground substance of the intima increasing its permeability

The presence of abnormal lipoproteins with particular biophysical properties has certainly been demonstrated in atherosclerosis but whether these are best adapted to penetrate the intima and be prevented from passing through the internal elastic lamina is as yet unknown Certainly also atherosclerosis is twice as frequent in hypertensive subjects as in those with normal blood pressures (Wilens 1947) There is evidence that most atherosclerotic lesions are preceded by some change in the ground substance of the intima and by subendothelial fibroblastic proliferation (Moon and Rinehart 1952) A certain degree of protection against cholesterol induced atherosclerosis in rabbits and chicks is afforded by both potassium iodide and thyroid hormone whether the blood lipids are favourably influenced by these substances or not (Katz and Stamler 1953) it has been suggested that this favourable effect is due to the decreased permeability of the vascular endothelium which is known to follow the administration of these drugs

ANGINA PECTORIS

Physiology Angina pectoris and its close relative the pain of intermittent claudication are believed to be due to certain metabolites that are formed in ischæmic working muscle (Lewis 1934) Whatever the precise explanation for the development of pain there can be no doubt that attacks depend upon relative myocardial ischæmia an idea first enunciated by Parry (1799) The term angina pectoris is customarily applied to transient pain only and refers to ischæmic attacks provoked by temporary stress during which the metabolic demands of the myocardium are beyond the capacity of the coronary circulation

Such a situation may arise during effort (1) if the coronary vessels are more or less occluded either at their mouths as in syphilitic aortitis or during their course as in atherosclerosis various forms of angiitis and embolism (2) if the coronary flow is diminished by other means such as aortic stenosis gross aortic incompetence tight mitral stenosis a high pulmonary vascular resistance or severe pulmonary stenosis (3) if the blood itself carries insufficient available oxygen as in anæmia or at high altitudes or (4) if the regular work of the heart is increased by such conditions as hypertension valve disease or hyperkinetic circulatory states

Although only angina pectoris resulting from coronary atherosclerosis concerns us here the other factors mentioned often play a contributory role thus anæmia may precipitate angina in a case of previously silent

coronary disease not only because of the limited oxygen transport, but also because the work of the heart is increased in order to maintain a high cardiac output Hypertension is particularly important in so far as it increases the work of the heart and contributes to the development of atheroma on the other hand it tends to iron out the plaques and so may prevent coronary narrowing in fact most cases of hypertensive heart disease have dilated coronary arteries (Harrison and Wood 1949) Clinically although more than half of all cases of ischæmic heart disease have blood pressures above 160/100 mm Hg (Cassidy, 1946) systolic pressures over 200 mm Hg are rare (Riseman and Brown 1937)

CLINICAL FEATURES

Angina is a symptom and must be distinguished from other pains in the upper half of the body by a careful analysis of its qualities and behaviour

Site The pain is central mid sternal and tends to radiate bilaterally across or round the chest into the sides of the neck and jaws or even into the face or nose into the shoulders and down the inner or outer sides of the arms sometimes as far as the little fingers or thumbs occasionally through to the back between the shoulder blades (fig 15 02) This full distribution was experienced by John Hunter (1796) It is not situated in the left inframammary area although it may be more left pectoral than sternal Radiation may be unilateral and it is true that the left side then suffers more often than the right, but it must not be thought that spread down the left arm is either especially typical or diagnostic for bilateral spread is more typical and many other pains may radiate down the left arm including left inframammary pain Although centrifugal spread is the rule radiation is occasionally centripetal the pain starting in the wrists upper arms or face and spreading thence to the chest Pain may even be confined to one of the points of radiation e g to the face back or wrist not being felt in the front of the chest at all

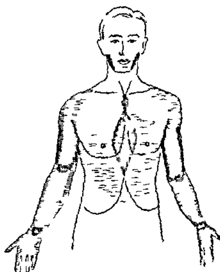


Fig 15 02—Diagram illustrating radiation of pain in ischæmic heart disease

Character Angina pectoris is classically constricting squeezing pressing or crushing, it is sometimes stinging numbing or burning sometimes it

cannot be described adequately by the patient It is not sharp shooting or stabbing which are the usual adjectives applied to left inframammary pain An important characteristic is its constancy the pain being steady while it lasts apart from initial waxing and final waning no pain which repeats itself in a succession of jabs or knife like thrusts is angina

Duration Attacks are measured in minutes usually they last two or three minutes occasionally five or ten they are not momentary, nor do they continue for hours and any pain that behaves in either of these ways is not angina pectoris (as defined above)

Provocation Angina is characteristically produced by any effort that increases the metabolic demands of the myocardium beyond the capacity of the coronary circulation and patients often know or learn the precise amount of effort necessary to provoke pain When the critical point is reached the patient usually feels compelled to stop whatever he is doing and to stand still until the pain passes off Attacks are brought on especially by walking uphill or against the wind by hurrying after meals by going out of a warm room into the cold or by any unaccustomed exercise less so by manual work to which the subject is trained Pain may also be induced by excitement anger fear or apprehension In advanced cases pain is provoked by lying down (angina decubitus) or stooping tending to occur when the patient first gets into bed at night or waking him from sleep It may then depend upon the rise in cardiac output that follows change of posture from vertical to horizontal or upon anxiety dreams

Pain that occurs after effort but not during it or that is provoked by lying on the left side or by the adoption of some particular posture (other than stooping or lying) is not angina these features are characteristic of left inframammary pain

The degree of angina pectoris (grade of effort intolerance) may be assessed according to the speed with which the patient is able to walk—not the distance In grade I pain is only provoked by hurrying or walking up hills or several flights of stairs in grade II walking on the level at an average speed causes pain usually within the first 300 yards in grade III pain occurs even when walking slowly and in grade IV there is pain at rest and total incapacity

As implied above patients with moderate angina usually complain of pain soon after the beginning of effort or not at all (Kemball Price 1951) if they do not have pain in the first quarter mile then can very likely walk indefinitely at the same speed Again if the pain is not severe patients can often walk it off This behaviour is presumably related to the effect of exercise on vasomotor tone i e to second wind

DIAGNOSIS OF ANGINA

If a pain conforms in site quality duration and relation to cardiac work to the features mentioned above it is angina pectoris and the diagnosis

must stand under any conditions except malingering The diagnosis should stand likewise when pain conforms to the required features in three out of the four respects mentioned provided it is not untenable in the fourth For example if a constricting pain brought on only by exertion and lasting but two or three minutes is localised in the left inframammary area it is probably not angina for the site makes the diagnosis untenable even though it conforms in the other three respects On the other hand if the same pain is situated in the left pectoral region between breast and clavicl it is almost certainly angina because this site though atypical is not contradictory Again a midsternal pressing pain brought on only by effort but lasting fifteen minutes is probably angina for the long duration though unusual is not altogether conflicting but should it last two hours it is not angina as defined above

It is sometimes said that certain associated symptoms such as breathlessness dizziness or faintness flushing sweating weakness and a feeling of impending death help to confirm the diagnosis It cannot be stressed too strongly that these symptoms carry little weight, for they are vasomotor in origin and although they may be provoked by an attack of angina they are in no way characteristic of it and are much commoner in the anxiety states*

The differential diagnosis includes anxiety states functional disorders or organic disease involving the dorsal spinal ligaments œsophageal or gastric spasm or distension diaphragmatic hernia and conditions causing respiratory distress

Anxiety states with left inframammary pain present no diagnostic difficulty but when pain is parasternal or even central it may be very confusing The patients are usually women near the menopause and they may describe a central pain radiating to the throat jaws and arms during or after effort when reaching up to a high shelf when washing or using the arms in other ways, and sometimes when emotionally upset As noted by Cassidy (1946) the attacks are apt to be widely spaced unrestricted effort causing no distress between them Complete investigations may reveal nothing significant in any system and the nature of the attacks remains obscure Angina can only be excluded and then with some uncertainty by obtaining a normal electrocardiogram during spontaneous or induced pain

Referred pain from the dorsal spinal ligaments may be felt across the front of the chest as in the experimental work of Lewis and Kellgren (1939) Attacks may be related to posture or reproduced by spinal movements or pressure over the interspinous ligaments from D2 to D4

Œsophageal spasm may cause central chest pain radiating down both arms and tight or bursting in quality There is no close relationship to effort and bouts may be periodic like any other gut colic The diagnosis may be proved by demonstrating œsophageal spasm by means of fluoroscopy and by obtaining a normal electrocardiogram during attacks (Wolferth and Edeiken 1942)

Diaphragmatic hernia may cause pain on effort similar to angina pectoris but attacks also occur without provocation especially when the patient lies down and at times even strenuous effort may be symptom free Severe attacks may be mistaken for cardiac infarction The diagnosis is made by means of a barium meal fluoroscopy being carried out with the patient tilted head down (Dwyer, 1937)

Relief of pain by belching in any disorder of the œsophagus or stomach is less helpful in distinguishing such conditions from angina pectoris than might be supposed for ischæmic pain may be similarly relieved in about 10 per cent of cases (Riseman and Brown 1937) Pain after meals is also common in cases of angina pectoris although slight effort may be necessary to provoke it

Bronchial asthma or extreme dyspnœa from any cause may be associated with a feeling of substernal tightness that should not be confused with angina pectoris for breathlessness is not a feature of transient myocardial ischæmia

PHYSICAL EXAMINATION

Having made the diagnosis on historical grounds the patient should be examined with a view to ascertaining the cause of the ischæmia Aortic valve disease and severe anæmia should be recognised by their characteristic features the presence of obesity or of hypertension noted the mental state of the patient assessed and attention should be paid to any other factor that may have a bearing on the frequency or severity of attacks In this respect, diabetes mellitus and polycythæmia must be borne in mind In the majority of cases however there are no physical signs the rhythm is normal the heart is not enlarged there are no murmurs and there is no evidence of congestive failure the peripheral and fundal arteries and the blood pressure may provide no evidence of general vascular disease fluoroscopy shows a heart shadow normal in size shape and pulsation and the electrocardiogram may be normal at rest It is repeated for emphasis that this apparent normality of the cardiovascular system is typical of pure angina pectoris due to coronary atherosclerosis and that with few exceptions physical signs radiological changes or electrocardiographic abnormalities are due to complications or associated disease even the demonstration of peripheral atherosclerosis proves little for it is common enough without serious involvement of the coronary vessels, and is often missing with advanced coronary disease

SPECIAL TESTS

Most of the special tests are of little help for the circulation is usually normal at rest Effort tolerance tests based on the behaviour of the pulse rate and venous pressure are of no value Reproduction of pain by prescribed effort for purposes of accurate analysis is sometimes useful with a

bad witness or pain may be induced to ascertain the prophylactic or curative effect of trinitrin The only reliable test, however, is to obtain an electrocardiogram immediately after effort (Scherf and Goldhammer 1933) when characteristic depression of the RS T segment with or without inversion of the U wave clinches the diagnosis (fig 15 03) The depression should measure 1 mm or more below the level of the atrial T wave and should remain flat or slope downwards for at least 0 08 second A depressed RS T junction followed by an upwardly sloping RS T segment is normal The best method is to make the patient exercise until he is in pain if he stops on account of fatigue or breathlessness without developing pain angina is unlikely* In the author s experience (Wood *et al*, 1950) only 5 per cent of electrocardiograms remain normal during or immediately after an attack of true angina or after sufficient effort to cause breathlessness and fatigue (in ischæmic subjects)

This test is not entirely without danger and should only be carried out when the diagnosis is really in doubt and the resting electrocardiogram normal or equivocal

The other method is to take serial electrocardiograms while the patient breathes 10 per cent oxygen for twenty minutes or for a shorter time if pain is produced As depression of the RS T segment occurs in normal subjects with this test a positive result is only accepted if the depression exceeds 2 5 mm in any lead or if the T wave becomes inverted in left ventricular surface leads or their counterparts (Larsen 1938 Levy *et al* 1938 1939 1941) The test is positive in 3 to 5 per cent of normal control (Biorck 1946 Weintraub and Bishop 1947) in 15 to 20 per cent of cases of doubtful angina and in 50 to 55 per cent of cases of undisputed angina (Levy *et al* 1941 Biorck 1946) In the opinion of the writer this test is less useful than the effort test being more difficult to carry out more difficult to interpret more dangerous, and far less frequently positive The subject is well reviewed by Stewart and Carr (1954)

COURSE

The onset of angina pectoris is more often sudden than gradual and is usually due to a small coronary thrombosis insufficient to cause cardiac infarction The patient may say he was capable of climbing mountains a week ago yet now he can scarcely walk 100 yards Less commonly pain is first experienced during unusually heavy exertion and gradually becomes more easily provoked This represents the slow development of occlusive atherosclerosis

The subsequent course is apt to be punctuated by short periods of relatively sudden deterioration followed by long periods of gradual improvement these episodes signify thrombotic occlusion of a medium sized coronary artery followed by the development of a collateral circulation (Schlesinger 1938) and perhaps by recanalisation

Sooner or later in the majority of cases thrombosis occludes one of the

V_R I V_L

(a) AT REST

(b) AFTER EFFORT

Fig 15 03—Electrocardiogram (a) before and (b) after exertion in a case of angina pectoris the control record (a) is practically normal the second record (b) shows significant depression of the ST segment

main coronary arteries and cardiac infarction results but a major thrombosis may occur without infarction, infarction may occur without thrombosis and ventricular fibrillation may terminate the illness in the absence of both (Appelbaum and Nicolson 1935 Nathanson 1936)

Angina may cause total incapacity in really severe cases and may finally occur at rest (status anginosus or acute coronary insufficiency)

Some cases severe or otherwise, improve after cardiac infarction others *lose their pain on developing congestive heart failure It is not clear why* this should be so but the explanation may be related to the fact that ligation of the coronary vein appears to improve the coronary circulation (Beck and Mako 1941)

PROGNOSIS

The average life expectancy from the onset of angina pectoris is nine to ten years (*White Bland and Miskall 1943*) *about 10 per cent* live well ... twenty years, e g John Hunter 1773–93, Sir James Mackenzie, 1907 ... Sir Thomas Lewis 1927–45 Of 6 882 cases followed for 5 to 23 years at the Mayo Clinic the mortality was 15 per cent in the first year and 9 per cent per annum thereafter (Block *et al* 1952) Women have a better prognosis than men and subjects over 40 years of age at the onset fare better than those under 40 (Parker *et al* 1946) Cardiac infarction hypertension enlargement of the heart changes of rhythm bundle branch block and other electrocardiographic abnormalities (at rest) all influence the prognosis adversely (Montgomery Dry and Gage 1947)

TREATMENT

Conservative The majority of patients with uncomplicated angina of mild or moderate severity are able to carry out sedentary or light manual work Any mental or physical activity that increases the frequency of attacks or that causes pain directly should be avoided whilst adequate rest and relaxation should be assured Diet should be light and its fat content low although hypercholesterolæmia is difficult to influence by such means atherogenic macromolecular lipoproteins of the S_f 10–20 class tend to be inhibited (Gofman *et al* 1950) Alcohol in moderation is not harmful in fact as a vasodilator it may be beneficial although it does not prevent electrocardiographic S T segment depression on effort (Russek *et al* 1950) Contributory factors such as hypertension obesity anæmia diabetes mellitus and anxiety should be corrected as far as possible

Cigarette smoking should be limited to 10 to 15 per day or given up altogether if it is found to precipitate attacks Intravenous nicotine bitartrate (2 mg) equivalent to five inhalations from a cigarette in one minute quickens the heart rate by about 15 beats per minute raises the blood pressure by an average of 12/8 mm Hg increases the cardiac output 1 to 2 litres per minute, and frequently causes dizziness or ...

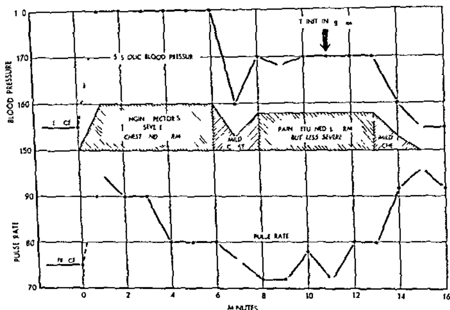


Fig 15 04—Graph showing close correlation between the height of the blood pressure and the degree or extent of pain during an attack of angina pectoris treated with trinitrin

faintness in ischæmic cases angina pectoris is provoked in 8 per cent and the electrocardiogram significantly altered in 12 per cent (Boyle *et al* 1947) Smoking cigarettes also inhibits diuresis an effect that has been attributed to stimulation of the posterior pituitary (Walker 1949) liberation of vasopressin (pitressin) may also explain the prolonged reduction of coronary blood flow that occurs in dogs (Bulbring Burn and Walker 1949) Since ischæmic heart disease is now alleged to be at least one and a half times more common in cigarette smokers than non smokers it may be wise to abandon the habit altogether As with lung cancer cigars and pipe smoking seem relatively innocuous

Trinitrin 1/100 to 1/120 of a grain (0 5 mg) introduced by Murrell in 1879 may be slipped under the tongue as required either to relieve an attack or before some unavoidable effort which might induce one Trinitrin is absorbed quickly through the oral mucosa and acts as a coronary vasodilator relieving pain without necessarily altering the blood pressure (Wayne and Laplace 1933–34) but if the blood pressure is lowered as well so much the better (fig 15 04) Ischæmic S T depression in the electro cardiogram is corrected quickly (fig 15 05) Trinitrin tablets (B P) deteriorate with age losing about 10 per cent of their potency per annum preparations such as angised (B W) and nitrocine (M C) overcome this drawback

Amyl nitrite 5 minims (0 3 ml) is also effective but less convenient (fig 15 06) a capsule may be broken in a handkerchief and inhaled the noise of the procedure the pungent smell of the vapour and the

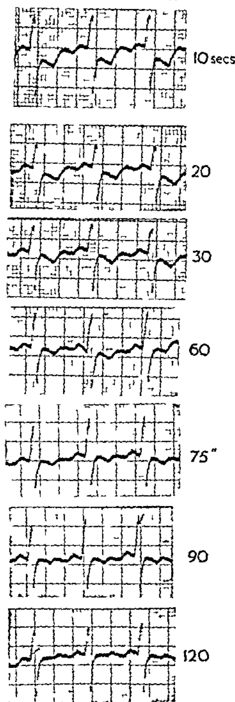


Fig 15 05—Graph illustrating rapid correction of ischæmic depression of the S T segment in lead V, in a patient with angina pectoris by means of trinitrin

vivid facial flush that accompanies its use are apt to embarrass the patient in public Amyl nitrite is a powerful vasodilator and relief of pain i associated with considerable tachycardia and conspicuous elevation of the cardiac output Much interest is also attached to the frequent paradoxical effect of amyl nitrite on the electrocardiogram for the depression of the S T segment that occurs during an attack of angina often becomes further depressed when the drug is inhaled and pain passes off (fig 15 07)

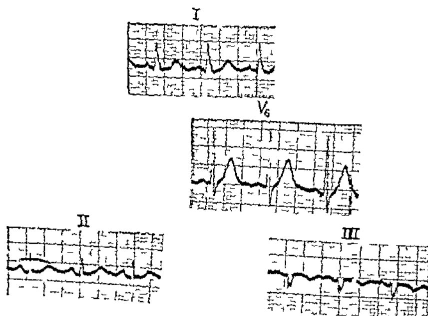
Few of the drugs used as longer acting coronary vasodilators are of much value (Master Jaffe and Dack, 1939) *Aminophylline* has the best reputation and is employed widely in doses of 0 1 to 0 2 G t d s It is difficult to demonstrate a physiological effect with such doses but severe angina may be relieved by 0 3 G four hourly if the patient can tolerate it Epigastric pain and nausea prohibit larger doses Aminophylline however may be given in conjunction with aluminium hydroxide as *theodrox*, and in this form 0 G is usually well tolerated Theophylline may also be given as *etophylate* this is the neutral salt of theophylline ethanoic acid and the base diethylene diamine and may be taken orally in doses of 0 25 to 0 5 G t d s without dyspepsia *Choline theophyllinate* in oral doses of 0 2 to 0 5 G t d s is also said to be well tolerated

V_R I V_L

V_1 V_2 V_3 V_4 V_5 V_6

II V_F III

AT REST



AFTER AMYL NITRITE

Fig 15 06—Electrocardiogram during an attack of myocardial ischæmia treated with amyl nitrite
Expected response showing prompt correction of the depressed S T segment

Amongst the long acting nitrites and nitrates there is *pentaerythritol tetranitrate* (nitropent) which has a mild coronary vasodilator action lasting for about four hours In Great Britain it is marketed as mycardol (Bayer) and peritrate (Warner) the former is made up in 30 mg tablets the latter in 10 mg tablets In oral doses of 10 to 30 mg one hour before meals nitropent not only tends to relieve pain but also inhibits electrocardiographic S T segment depression on exercise (Russek *et al* 1953) Larger doses of nitropent usually cause dyspepsia

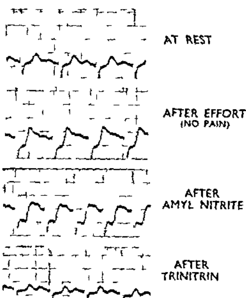


Fig 15 07—Paradoxical effect of amyl nitrite on depression of the S T segment in a case of angina pectoris

Recent reports have claimed that khellin an extract from the seeds of an Eastern Mediterranean wild plant *ammi visnaga* is an effective coronary vasodilator with a prolonged action The dose is 100 mg by mouth three times daily Angina pectoris is said to be relieved in 74 per cent of cases (Anrep *et al* 1946 1947) Unfortunately khellin is so badly tolerated by the majority of patients that in its present form it can hardly be considered a therapeutic agent

Enthusiastic reports from Canada concerning the beneficial effect of vitamin E in doses of 200 to 600 mg (Shute 1945) have not been confirmed

Since *œstrogens* not only inhibit experimental atherogenesis in cockerels but also reduce the severity of atherosclerotic lesions already present (Katz and Stamler 1953) they have naturally been tried therapeutically in man and as previously stated they tend to restore the normal blood lipid pattern (Barr 1953) Improvement of ischæmic heart disease however has not yet been demonstrated and the side effects such as mammary development in the male are undesirable There may be a stronger case for the use of œstrogens in cases of angina pectoris in relatively young women who have undeveloped ovaries or who have had bilateral oophorectomy

Testosterone propionate has no place in the treatment of angina pectoris for androgens are contra indicated

Other agents that may inhibit atherogenesis or actually help to clear lesions already present are under trial they include inositol (Felch *et al* 1952) beta sitosterol (Barber and Grant 1955) and heparin (Engelberg 1952) No such drug can yet be recommended therapeutically

Artificial myxœdema Total ablation of the thyroid gland was introduced

by Blumgart Levine and Berlin (1933) in the hope that an appreciable reduction on the circulatory demands would benefit cases of angina pectoris (and congestive heart failure) Fair results were obtained (Cutler and Schnitker 1934) improvement being partly attributed to decreased sensitivity to adrenaline (Eppinger and Levine 1934) The operation gained little favour in England The high blood cholesterol that results does not favour the natural course of the disease and the doubtful benefits obtained hardly justify the risks and complications of total thyroidectomy

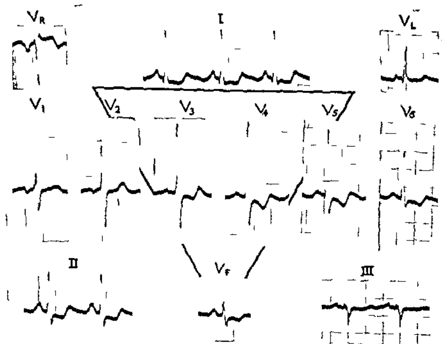


Fig 15 08—Acute coronary insufficiency showing persistent inversion of the S T segment in all indirect surface leads

Thiouracil however offers a simple and more easily controlled means of achieving the same object and can be abandoned at any time if the result is unsatisfactory (Raab 1945 Ben Asher 1947) The dose recommended is 200 to 600 mg of methyl or propyl thiouracil daily beginning with the larger dose and gradually reducing it to the minimum that proves effective If more heroic doses are required equal quantities of propyl and methyl thiouracil may be given together in the hope of avoiding toxic reactions such as fever rash and agranulocytosis the principle being that drug combinations (e g sulphonamide mixtures) cause less sensitisation than the same total dose of a single member of the group while retaining the same therapeutic effect (Lehr 1948) Cases of severe angina pectoris do not tolerate thiouracil fever well In the experience of the author fever and

rash are less common with propyl than with methyl thiouracil Mercazole 20–30 mg three times daily, finally reduced to about 10 mg t d s is equally effective and seems relatively free from complications

The blood cholesterol should be watched and if it rises above 300 mg per cent the question of reducing the dose of thiouracil or mercazole should be considered A low fat diet may help to keep the blood lipids within bounds

Radioactive iodine (I^{131}) performs the same service as thyroidectomy and is equally permanent It may be given in a single dose of 20 millicuries or in three divided doses of 10 millicuries at weekly intervals The B M R may then be maintained at minus 20–25 per cent by means of small doses of thyroid In view of the poor prognosis in these difficult cases the danger of late malignancy may be disregarded In their latest review of 7 0 resistant cases of angina pectoris treated by means of artificial myxœdema Blumgart *et al* (1955) reported a good result in 75 per cent I have never myself been able to develop much enthusiasm for this form of treatment partly because of the rise in blood cholesterol that usually takes place and partly because it is very difficult to keep patients relatively free from pain without provoking distressing features of myxœdema but then I have o ly embarked on antithyroid treatment in advanced cases that have been almost totally incapacitated

Surgical methods Several surgical procedures designed to relieve angina have been evolved in recent years Few have gained much support but there is something to be said in favour of abolishing pain by sensory denervation of the heart achieved by means of section of the upper four dorsal spinal nerve roots or by stellate and upper dorsal ganglionectomy (White Garrey and Atkins 1933) Destruction of the ganglia by alcoholic injection is less certain and may cause intractable root pain in about 10 per cent of cases Despite the theoretical argument that ganglionectomy may remove nature s warning signal and so allow patients to exercise themselves beyond the limits of safety there is no doubt tha some cases do remarkably well (White and Bland 1948 Lindgren 1950) Sensory denervation of the heart does not entirely abolish the subjective recognition of an anginal attack although the sensation experienced is not painful There is good reason to believe also that sympathectomy tends to prevent ventricular fibrillation (Leriche *et al* 1931, McEachern 1940), and seems to improve the coronary circulation either by preventing reflex spasm (Levy and Moore 1941) or by causing coronary vasodilatation (Katz and Jochim, 1939)

A more drastic surgical procedure aims at improving the coronary circulation by supplying it with a new source of collateral vessels The idea was based on necropsy observations which showed that the heart might function remarkably well despite almost complete coronary occlusion if for some reason an adequate collateral circulation had developed through the pericardium These natural results of accident and disease have been mar

shalled and developed by Claud Beck (1935–36) in the U S A and by O Shaugnessy (1936–37) in England Beck sutured a flap of pectoral muscle to the surface of the heart O Shaugnessy preferred cardio omentopexy the omentum being brought up through the diaphragm and stitched or glued on to the surface of the heart after scarification Whilst experimental evidence affords convincing proof of the establishment of a collateral circulation by such means the results obtained in clinical cases of ischæmic heart disease scarcely justify the risk entailed

A simpler means of achieving the same object is to introduce bone dust into the pericardial sac when the pericardial reaction subsides vascular adhesions offer a collateral source of blood supply to the myocardium (King 1941) Powdered magnesium silicate serves equally well (Thompson and Plachta 1953)

ACUTE CORONARY INSUFFICIENCY

The term *acute coronary insufficiency* (Master *et al* 1947) is now widely used to describe those cases of ischæmic heart disease that cannot properly be called angina pectoris or cardiac infarction but rather something between the two Some cases are subacute or even chronic

Physiologically the coronary circulation is insufficient to meet the full demands of the myocardium at rest, yet sufficient to prevent myocardial necrosis Since the situation commonly develops relatively suddenly it is usually attributed to coronary thrombosis or possibly to subintimal hæmorrhage

Special forms of acute coronary insufficiency may be caused by any agent that temporarily interferes with the coronary blood flow e g hæmorrhage (Master *et al* 1950) shock (Wiggers 1947) vaso vagal syncope asphyxia and carbon monoxide poisoning especially if the work of the heart is increased simultaneously as in paroxysmal tachycardia atrial flutter (or fibrillation) massive pulmonary embolism and ruptured aortic cusp greatly increased cardiac work alone may also cause coronary insufficiency (especially when there is latent coronary disease) as in hypertensive or thyrotoxic crises

Clinically the onset is usually acute or subacute from a state of normal or relatively good health the patient suddenly finds himself unable to walk more than a few yards without pain and may have prolonged attacks of angina at rest particularly after food and when he lies flat but the pain is still relieved by trinitrin there is no fever leucocytosis elevation of the sedimentation rate or increased transaminase activity the blood pressure does not fall there is no pericardial friction or other clinical evidence of cardiac infarction and the electrocardiogram shows nothing more than ischæmic depression of the RS T segment in left ventricular surface leads or their equivalents (fig 15 08) These electrocardiographic changes usually persist for several days or weeks and are not confined to attacks of pain

Fig 15 9—Transient inversion of the T waves in all chest leads in a case of acute coronary insufficiency

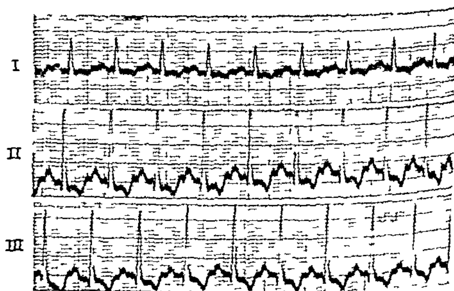


Fig 15 10—Electrocardiogram showing transient inversion of the T waves following prolonged circulatory collapse with extreme tachycardia without evidence of structural disease of the heart

Transient inversion of the T waves proper, without abnormal Q waves and without elevation of the RS T segment may also occur in coronary insufficiency (fig 15 09) but is more difficult to interpret for it is also compatible with a small cardiac infarction Simple transient inversion of the T waves is common in the special forms of coronary insufficiency mentioned above (fig 15 10) especially following prolonged paroxysmal tachycardia in paroxysmal hypertension from pheochromocytoma and in carbon monoxide poisoning (fig 15 11)

Treatment

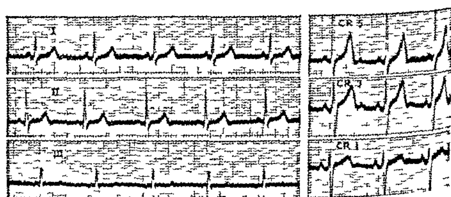
Patients with acute coronary insufficiency should be put to bed for a minimum period of three weeks and treated with anticoagulants (page 746) in order to prevent extension of thrombosis the fear that a subintimal hæmorrhage may be aggravated by such treatment is not substantiated in practice Treatment should be continued for at least three weeks after attacks of pain have ceased which may mean for two to three months in obstinate cases These prolonged subacute cases may be very trying to all concerned and it might seem better to abandon treatment in the hope that the ischæmic zone would then necrose and the pain cease While it is agreed that this may happen and the patient be the better for it it is unfortunately impossible to predict the consequences which are just as likely to be disastrous Controlled cardiac infarction is beyond our present therapeutic powers It is far better therefore to continue anti coagulant treatment with or without the temporary help of an antithyroid drug, for sooner or later the situation is likely to ease as the result of an improved collateral circulation

That anticoagulant therapy alters favourably the immediate outcome and future course of cases of acute coronary insufficiency has not yet been proved but I have little doubt that it does Cardiac infarction is preceded by symptoms of acute coronary insufficiency in at least one quarter of all cases (Mounsey 1951) of a personal series of 25 cases of acute coronary insufficiency not treated with anticoagulants no less than 12 developed acute cardiac infarction within three weeks and five of these died of 33 similar cases treated with anticoagulants only two developed cardiac infarction within the month neither of which died and a third steadily deteriorated and died suddenly a week after the onset of treatment Both series are small because the criteria on which the diagnosis was based were strict (Wood 1948)

Prognosis

Long term follow up studies of cases proved at the time to have acute coronary insufficiency rather than cardiac infarction await analysis The immediate outcome depends largely on whether cardiac infarction develops or not as explained above Less than 5 per cent die abruptly from ventricular fibrillation without infarction

(a) Third day



(b) Twelve days later

Fig. 1 11.—Transient inversion of the T waves due to carbon monoxide poisoning

CARDIAC INFARCTION

Myocardial infarction occurs when a mass of heart muscle is sufficiently deprived of its blood supply for an adequate time. The common cause of such an event is coronary thrombosis, but coronary embolism, subintimal hæmorrhage in an atherosclerotic vessel, dissection, and critical lowering of the blood-pressure, as from shock or hæmorrhage, in a patient with occlusive coronary atherosclerosis or syphilitic aortitis may each produce it. Again, coronary thrombosis does not cause myocardial infarction if the collateral circulation is sufficient to preserve the life of the threatened tissue. It follows that coronary thrombosis and myocardial infarction are

not synonymous terms and should not be confused the former means no more than its literal sense implies the latter means death of a localised mass of heart muscle

ANATOMY OF THE CORONARY CIRCULATION

The site and extent of the infarct depend upon the vessel or vessels occluded upon the capacity and efficiency of collateral channels and upon the anatomy of the coronary circulation

There are two main coronary arteries left and right The left divides early into an anterior descending branch and into a left circumflex the large anterior descending branch runs down the interventricular groove to the apex of the heart and nourishes the anterior part of the right ventricle the interventricular septum and the anterior and apical part of the left ventricle the smaller left circumflex branch curls round the back between the left atrium and ventricle and supplies the upper lateral and posterior basal portion of the left ventricle The right coronary artery does not divide but runs round to the back between the right atrium and ventricle sending branches to the region of the sinus node to the anterior part of the right ventricle and to the posterior base of both ventricles There is a considerable degree of anastomosis between the terminal branches of these vessels an anastomosis that increases rapidly when the blood supply to any area is threatened (Prinzmetal *et al* 1947) The right ventricle supplied as it is by the two biggest coronary arteries and offering little resistance to systolic coronary blood flow is rarely the seat of infarction The upper and lateral part of the left ventricle is supplied by proximal branches from both anterior descending and left circumflex vessels and is therefore relatively safe The posterior basal region is less secure for it is supplied only by terminal branches, some from the right coronary artery and some from the left circumflex In having this double source of nourishment however it is still more fortunate than the anterior apex of the left ventricle which is fed almost entirely by terminal rami from the anterior descending branch of the left coronary artery although anastomotic channels can develop rapidly from the posterior descending branch of the right coronary artery The interventricular septum is supplied anteriorly by perforating branches from the anterior descending coronary artery and posteriorly by perforating branches from the right Anastomoses are more conspicuous in the superficial layers of the myocardium than in the inner layers (Prinzmetal *et al* 1948) they are also at a physiological disadvantage when near the endocardium because they are subjected to a higher intramyocardial pressure (Johnson *et al* 1939)

SITE OF THROMBOSIS AND INFARCTION

Clinically major coronary thrombosis involves the anterior descending branch of the left coronary artery in 66 to 75 per cent of cases the right coronary artery in 25 to 40 per cent and the left circumflex in 5 to 33 per cent (Barnes and Ball 1932 Appelbaum and Nicolson 1935 Munck,

1946) *thrombosis of the left main trunk is relatively rare* These figures are conservative for careful study of the whole coronary tree by means of radio opaque injections reveals multiple thromboses in the majority of instances

The relative incidence of the various sites of infarction harmonises with the anatomical and physiological data and with the sites of thrombosis In an analysis of 160 cases Wartman and Hellerstein (1948) found chiefly anterior infarction in 72 per cent and chiefly posterior infarction in 8 per cent but there were multiple infarcts in 41 per cent Half the anterior infarcts and a quarter of the posterior infarcts also involved the inter ventricular septum Right ventricular infarction rarely occurs alone but may complicate anteroseptal infarction of the left ventricle (Zaus and Kearns 1952) *Atrial infarction has also been described* (Hellerstein 1948)

Combining figures published by Appelbaum and Nicolson (1935) Nathanson (1936) Clawson (1939) and Munck (1946) it is found that *coronary thrombosis occurs without cardiac infarction in 20 per cent* of cases and that cardiac infarction occurs without coronary thrombosis in 29 per cent *in the latter group atherosclerotic occlusion may be complete* or incomplete

PATHOLOGY

A cardiac infarct may be difficult to distinguish with the naked eye when less than twenty four hours old microscopically however *acute necrosis* of the muscle fibres may be recognised by their swollen appearance and by the loss of their nuclei and striations When a few days old an infarct is discoloured and may be surrounded by a red zone of hæmorrhage or congestion Microscopically the necrosed muscle is seen to be invaded by polymorphs Older infarcts are yellowish white in colour *and represent* scar tissue

When necrosis involves the inner layers of the myocardium mural thrombi frequently form against the damaged endocardium in fact they are found in 40 to 50 per cent of all cases (Hellerstein and Martin 1947) Local pericarditis occurs over superficial necrosis and *has been reported* in 30 to 75 per cent of all cases (Wartman and Hellerstein 1948 Stewart and Turner 1938) diffuse pericarditis develops *in about 10 per* cent

Myocardial softening (myomalacia cordis) may result in rupture of the heart (5 to 15 per cent) or in the formation of a cardiac aneurysm (10 to 30 per cent according to published necropsy figures and according to the definition of an aneurysm)

Precipitating agents If due allowance is made for the average time occupied by sleep ordinary activities and physical effort during each twenty four hours then coronary thrombosis (at least in men under 4) occurs six times more frequently during physical effort than during sleep and twice as frequently during physical effort as during ordinary day to-day

activities (Yater *et al* 1948) Unaccustomed effort particularly, may precipitate an attack

The peak incidence of coronary thrombosis is in December (Brown and Pearson 1948) but according to Teng and Heyer (1955) is more related to sudden changes of temperature than to the cold *per se* Certainly going out into the cold after leaving a warm room very commonly provokes an attack of angina pectoris in ischæmic subjects Clearing the drive of snow includes both unaccustomed effort and the change from a warm to a cold temperature and is a known precipitating cause of coronary thrombosis

A heavy meal is often blamed but statistical evidence on the point is not available Sexual intercourse is in the same category Both are notorious causes of an attack of angina pectoris There is likewise as yet no proof that a prolonged period of excessive mental stress can be responsible although experience favours the view that it can

Other known precipitating agents include surgical shock the post operative state trauma and a sudden fall of blood pressure

SYMPTOMS

Although the onset of cardiac infarction is sudden premonitory symptoms are common during the preceding week or so and take the form of typical or atypical angina pectoris Then or without warning of any kind and often without any obvious precipitating cause the major attack overwhelms the patient and is commonly signalled by pain indistinguishable in site radiation and quality from angina pectoris but instead of passing off in a few minutes it lasts for hours Its intensity varies from a feeling of pressure to extreme agony and gives no indication of the size of the infarct There may be no other symptoms on the other hand there may be collapse weakness faintness sweating restlessness breathlessness and vomiting Whilst a classical attack is characterised by pain others present with syncope and yet others with suffocation In the syncopal type which represents a vaso vagal reaction loss of consciousness may prevent appreciation of pain when paroxysmal cardiac dyspnœa or acute pulmonary œdema dominates the scene the patient usually admits pain on close questioning The lack of agreement in the literature concerning the frequency of painless infarction (0–61 per cent) may be explained by the heterogeneous manner in which historical data is collected and by lack of uniformity with regard to the definition of the word *painless* In about one third of all cases patients deny pain in its ordinary sense preferring words like discomfort pressure tightness oppression or heaviness—as in angina pectoris Less than 5 per cent of cases of cardiac infarction have no ischæmic sensation at all about half of these are entirely silent and discovered by routine electrocardiography

PHYSICAL SIGNS

Unlike angina pectoris myocardial infarction provides a wealth of physical signs and special findings When first seen the patient is usually

grey cold sweating obviously ill and in pain he may be breathless and cyanosed or he may be pale and collapsed—perhaps unconscious on the other hand he may present none of these features Within two or three days mild cases may look and feel well

The jugular venous pressure is sometimes a little raised during the first day or two and the pulse rate accelerated but in cases with a vaso vagal reaction there may be bradycardia There may be orthopnœa paroxysmal cardiac dyspnœa or frank pulmonary œdema in severe cases

The *blood pressure* falls initially only in cases with a vaso vagal reaction and indeed may be elevated during the first twelve hours or so (Weiss 1939) *in animals it is similarly maintained for the first twenty four hours* (Gross *et al* 1938) but it drops later commonly reaching its lowest level on the third or fourth day, when systolic pressures of 80 to 90 mm of mercury are often found Thereafter it remains low for several days or even for weeks and then in all who survive climbs slowly back towards its previous level which it may or may not reach (fig 15 12) In 67 per cent of fatal cases Chambers (1947) observed no such recovery *In hypertensive subjects this drop in pressure may not be recognised unless the original* level is known

The *heart sounds* are often faint particularly when the blood pressure is low and there may be presystolic or diastolic gallop rhythm *Transient pericardial friction* is heard in about 10 per cent of cases especially when the infarct is anterior *Disturbances of rhythm* are not uncommon and include ectopic beats paroxysmal ventricular tachycardia auricular flutter or fibrillation and any grade of heart block

Low grade fever is the rule and may continue for several days but rarely for more than a week Transient polymorphonuclear *leucocytosis* also occurs *during the first few days and the C-reactive protein* test is positive The *sedimentation rate* begins to accelerate after a day or two reaches maximum velocity towards the end of the first week and then gradually returns to normal in an average period of six weeks from the onset (fig 15 13) (Wood 1936)

During the first 48 hours the *serum glutamic oxalacetic transaminase* (S G O T) activity is sharply increased from the normal of 10 to 40 units to any level up to 800 units the height to which it rises being proportional to the mass of necrosed myocardium (La Due *et al* 1954 1955) S G O T is an enzyme employed in the synthesis of glutamic and oxalacetic acid and is widely distributed in the tissues especially in heart muscle It is not increased in infectious neoplastic metabolic or degenerative diseases unless there is destruction of cardiac hepatic or muscular tissue

ELECTROCARDIOGRAPHIC APPEARANCES

These have already been described and explained in Chapter III Leads facing the surface of the *infarct show a prominent or monophasic* Q wave initial elevation of the RS T segment and subsequent inversion of the T

wave Anterior infarcts may be mapped out with precision by means of multiple unipolar chest leads and may be chiefly anterolateral (fig 15 14) or anteroseptal (fig 15 15) The Q T pattern is usually transmitted to lead V_L and hence mainly to standard lead I but if the heart is electrically vertical a V_5 Q T pattern may be transmitted to lead V_F and hence to standard leads II and III The Q T pattern of posterior infarcts is seen in œsophageal leads over the posterior surface of the left ventricle and is transmitted to lead V_F and hence to standard lead III (fig 15 16) while chest leads usually show initial depression of the RS T segment followed by unusually tall T waves (fig 15 17)

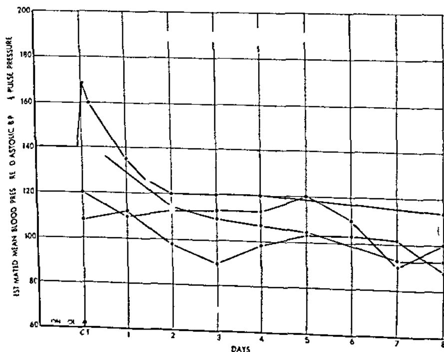


Fig 15 12—Behaviour of the blood pressure in four cases of acute myocardial infarction

The abnormal Q wave develops early and may persist indefinitely Elevation of the R T segment is usually transient but a monophasic Q wave associated with persistent elevation of the Q T egment is often seen with ventricular aneurysm (fig 15 18) Primary inversion of the T wave appears in a few days reaches a maximum within two or three weeks and then gradually reverts towards normal but slight inversion with Pardee coving of the RS T segment may persist in one or more leads (fig 15 19)

The diagnosis of acute cardiac infarction is practically untenable if serial electrocardiograms remain normal in all the recognised leads but an initial electrocardiogram may be normal occasionally if taken within a few hours

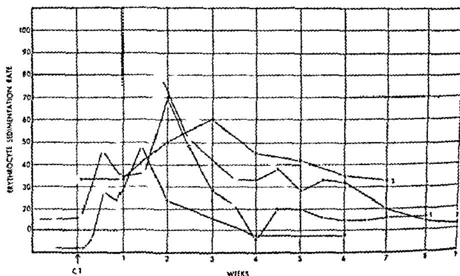


Fig 15 13—Behaviour of the sedimentation rate in four cases of acute myocardial infarction

Fig 15 14—Electrocardiogram showing anterolateral cardiac infarction Maximum changes are seen in leads V_3 V_4 V_L and standard lead I

of the onset This statement may have to be tempered in the light of Prinzmetal s evidence that the inner third of the myocardium may be electrically silent (Prinzmetal *et al* 1953) at least in respect of the initial

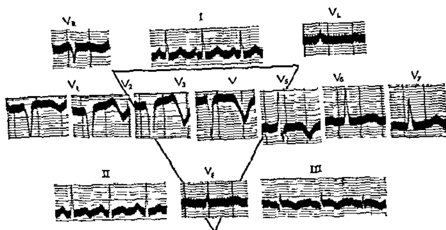


Fig 15 15—Electrocardiogram showing anteroseptal cardiac infarction Maximum changes are seen in leads V_3 and V_4

ventricular complex The belief that subendocardial infarcts cause depression of the RS T segment in overlying surface leads (Levine and Ford 1950) is not supported by Prinzmetal s experimental work (Rakita *et al* 1954)

In differential diagnosis great stress is laid on the abnormal Q wave for this always means appreciable necrosis of heart muscle however produced It must of course be distinguished from a normal Q wave measuring 2 or 3 mm and a monophasic downward deflection in standard lead III should not be accepted as a Q wave unless Q is also prominent in standard lead II and in lead V_F (fig 15 20) Pathological Q waves however *may* be seen occasionally in cases of myocardial necrosis caused by non ischæmic agents e g isolated myocarditis amyloidosis, tumour, hydatid, and other rare cardiopathies*

Elevation of the RS T segment is also seen in pericarditis and opposite large S waves in appropriate leads in left ventricular preponderance and left bundle branch block but the contour of the S T segment and the general pattern is different as described elsewhere

Primary inversion of the T wave alone is less conclusive evidence of infarction for it may be seen in a variety of conditions including toxic myocarditis pericarditis, carbon monoxide poisoning myxœdema, certain biochemical states most of the relatively obscure cardiopathies, and following paroxysmal tachycardia. However the depth and sharpness of the inversion usually exceed that in all other types and its association with upward coving of the RS T segment is practically diagnostic Changes in

Fig 15 16—Electrocardiogram showing posterior cardiac infarction Characteristic changes are seen in leads V_F and hence in leads II and III The ST segment is depressed in lead V_4

serial graphs are less helpful because many of the primary T wave changes mentioned above are also transient•

Bundle branch block mostly left occurred in 7 3 per cent of 700 cases of angina pectoris and in 8 9 per cent of 328 cases of cardiac infarction reported by Salcedo Salgar and White (1935) Conversely they found that ischaemic heart disease accounted for approximately 50 per cent of 181 cases of intra ventricular block of all types Master, Dack and Jaffe (1938) found the

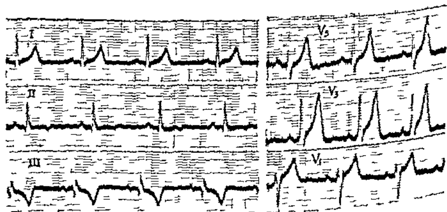
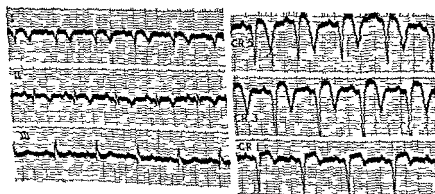


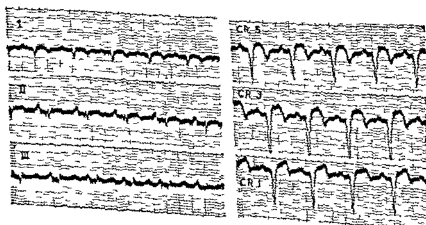
Fig 15 17—The later stage of posterior infarction showing unusually tall T waves in chest leads



(a) 29th November 1941



(b) 15th December 1941



(c) 3rd March 1942

Fig 15 18 Electrocardiogram showing widespread monophasic Q waves and persistent levation of the ST segment associated with ventricular aneurysm

Fig 15 19—Electrocardiogram of a case of old cardiac infarction showing persistent Q waves and Pardee coving of the ST segment in anterior left ventricular surface leads and their counterparts (leads V_L and standard lead I) The infarct occurred 14 months previously

Fig 15 20—Electrocardiogram in a case of pregnancy showing a prominent Q wave and inversion of the T wave in lead 3 due to cardiac rotation note the absence of a pathological Q wave in lead V_F and the presence of an S wave in standard lead I

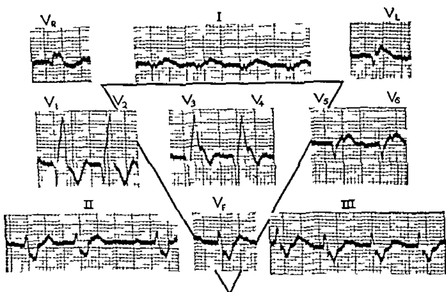


Fig 15 21—Electrocard ogram show ng typical appearances of anterior cardiac infarction in the pr sence of right bundle branch block

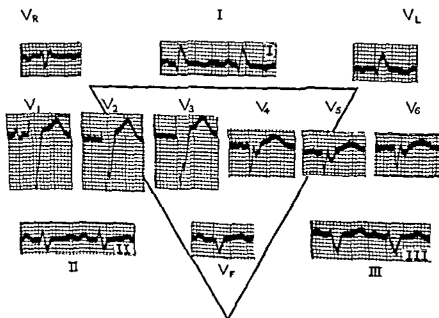


Fig 15 2 —Electrocardiogram showing typical appearances of anterior cardiac infarction in the presence of left bundle branch block

incidence of bundle branch block in acute coronary occlusion to be 1 per cent in 1,058 cases collected from the literature, and 15 per cent in 3,5 cases of their own Intraventricular block does not necessarily imply septal infarction in these cases and of course may precede the acute episode Its importance lies in the fact that it may mask the electrocardiographic signs of cardiac infarction for as explained on page 99 there can be no Q wave in leads facing the surface of the left ventricle in cases of left bundle branch block unless the septum is also necrosed and the gross deformity of the R T component may overshadow RS T changes due to the infarct Somerville and Wood (1949), however found that the characteristic Q T pattern of an infarct could be recognised in nearly all cases complicated by right bundle branch block (fig 15 21) and in about half those with left bundle branch block (fig 15 22)

Electrocardiography may be of great value in the diagnosis of myocardial infarction months or years after the event an abnormal Q wave, local dwarfing of R or primary inversion of the T wave in one or more left ventricular surface leads or their counterparts being particularly helpful Complete restitution of the normal electrocardiographic pattern occurs in only 10 per cent of survivors from acute myocardial infarction (Mills *et al* 1949)

RADIOLOGICAL FINDINGS

Fluoroscopy is impracticable during the acute stage of the illness but may be useful later An infarct on the left border of the heart near the apex may form a ledge (fig 15 23) In normal hearts pulsation is seen around the whole surface of the left ventricle in myocardial infarction there may be local absence of pulsation or pulsation may be locally paradoxical a portion of the ventricle expanding while the rest contracts this area of absent or paradoxical pulsation represents the infarct and may be seen on the left border of the heart towards the apex or on the diaphragmatic surface of the left ventricle (with the aid of gas in the stomach) for some reason posterior basal infarcts are less easily visualised Interpretation of pulsation as seen on the fluoroscope is by no means easy and requires considerable experience of normal variation The kymograph a simple device for obtaining a permanent skiagraphic record of cardiac pulsation has been used with some success as an aid in analysing the findings and the electrokymograph is even better but absence of pulsation at the apex may also be seen occasionally in hypertensive and other forms of heart failure

Ventricular aneurysm is more easily recognised particularly when situated towards the apex or left lateral border (fig 4 34) It should not be confused with a dilated left atrium an intrapericardial hæmatoma pericardial cyst or cardiac tumour Rarely a ventricular aneurysm may become calcified (fig 4 35) Increased density and unfolding of the aorta due

to atheroma with or without calcification may be seen in many cases, but cannot be regarded as evidence of coronary atherosclerosis calcified coronary arteries (Snellen and Nauta 1937) offer more convincing proof but even these do not necessarily signify ischæmic heart disease

Apart from the changes mentioned the size and shape of the heart are usually normal in cases of uncomplicated cardiac infarction (Miller and Weiss 1928) enlargement is commonly due to heart failure or to coincident hypertensive heart disease

With the aid of retrograde aortography via the right radial artery the entire coronary tree may be seen and the exact site of any obstruction identified (Coelho *et al*, 1953) but the method is certainly not without risk and cannot be recommended as a safe diagnostic procedure

COMPLICATIONS

(first 28 days)

	PERIOD (early mid or late)	FREQUENCY (per cent)	MORTALITY (per cent of all cases)
Abrupt death (ventricular fibrillation or asystole)	Onset Early or mid	?25 10	?25 10
Shock	Early	10 to 15	7 to 1[illegible]
Conventional heart failure	Mid and late	10 to 15	3 to 5
Rupture of heart of septum of papillary muscle	 Early Early Early	 1.5 to 3 Rare Rare	 1.5 to 3 Rare Rare
Cardiac aneurysm	Early (recognised late)	5 to 10	(See rupture those recognised commonly survive)
Pericarditis	Early	10	(See rupture majority survive)
Thrombo-embolism Pulmonary Systemic (chiefly cerebral)	 Mid and late Mid	 15 5 to 10	 2 to 3 1 to 2
Changes of rhythm Atrial fibrillation Atrial flutter or tachycardia Ventricular tachycardia Complete heart block	 Early Early Early Early	 10 2 2 1	Changes of rhythm increase the mortality from cardiogenic shock and heart failure
TOTAL (excluding abrupt death at onset)	—	—	25 to 30

COURSE AND COMPLICATIONS

The acute stage lasts on the average for six weeks during the earlier part of which many complications may arise (see table) the gravest danger being abrupt death from *ventricular fibrillation* (fig 15 24) About 10 per cent of all cases that survive long enough to be admitted to hospital die in this way and there must be many others that go to the coroner Thus of 866 cases in relatively young men reported by Yater *et al* (1948) 16 per cent died at once and another 10 per cent within 15 minutes none of these cases would have had time to be admitted to hospital If coroners cases are included therefore it is likely that at least one third of all cases of acute cardiac infarction die from ventricular fibrillation or asystole

Other disturbances of rhythm are also relatively common and include ventricular ectopic beats paroxysmal ventricular tachycardia (2 per cent), paroxysmal auricular flutter (2 per cent) and fibrillation (10 per cent) nodal rhythm and heart block They should be regarded seriously because *they may herald ventricular fibrillation or precipitate heart failure* Complete heart block (1 per cent) is particularly lethal (Mintz and Katz 1947)

Shock attending the first stage of acute cardiac infarction is characterised clinically by pallor sweating vomiting coldness of the extremities and exposed surfaces faintness or loss of consciousness great weakness, restlessness oliguria or anuria small pulse tachycardia or bradycardia and low blood pressure physiologically the cardiac output is much reduced the peripheral resistance raised the circulation time prolonged and the venous pressure raised (Freis *et al* 1952 Gilbert *et al* 1954) Fundamentally therefore there is a state of acute and severe heart failure although peripheral circulatory failure may complicate the picture and sweating *vomiting and a slow pulse rate suggest* powerful vagal activity Cardiogenic shock occurs in 10 to 15 per cent of cases and is fatal in two thirds to three quarters of them (Selzer 1952)

Heart failure may present more conventionally *either* as left ventricular failure or congestive heart failure Acute left ventricular failure with pulmonary œdema may occur at the onset or a more insidious form with dyspnœa and orthopnœa may develop later not *infrequently* during convalescence Congestive failure with a rise of venous pressure distension of the liver and œdema may also be a relatively late complication and increases the risk of phlebothrombosis and pulmonary embolism Conventional heart failure distinct from cardiogenic shock, usually responds to treatment in the first instance but is a common cause of death during the ensuing twelve months During the acute stage of cardiac infarction (first 28 days) it occurs as frequently as shock (10 to 15 per cent of cases) and *proves fatal in approximately 3 to 5 per cent* It is very difficult to obtain precise figures from the literature for cardiogenic shock and conventional heart failure are frequently grouped together

Thrombo embolic lesions in various situations *are detected* clinically in about 20 per cent of cases and may be found at necropsy in about 45 per



Fig 15 23—Skiagram in a case of anterior cardiac infarction showing a ledge on the left border of the heart

cent (Hellerstein and Martin 1947) The dangerous period is from the fifth or sixth day to the end of the third week, when the clotting time is shortened (Ogura *et al* 1946) Phlebothrombosis in the legs resulting in pulmonary embolism is by far the most common clinical manifestation and is responsible for death in 2 to 3 per cent of all cases of acute cardiac infarction In a series of 200 fatal cases of coronary thrombosis reported by Eppinger and Kennedy (1938) pulmonary embolism was directly responsible for death in 6 5 per cent was present in 24 5 per cent and complicated 32 7 per cent of those with heart failure The usual frequency of pulmonary embolism in all cases of cardiac infarction that survive long enough to be admitted to hospital is 15 per cent (Evans 1954)

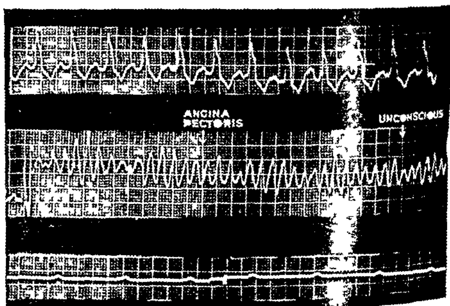


Fig 15 24—Electrocardiogram showing the mode of death in a case of ischaemic heart disease entricular fibrillation developed while a routine graph was being taken

Systemic embolism (or thrombosis) is detected *clinically* in 5 to 10 per cent of cases the majority of them cerebral Only 1 to 2 per cent of all cases of acute cardiac infarction die from cerebral or other systemic embolism Hellerstein and Martin give the actual incidence of various thrombo-embolic lesions as follows

	Per cent
Pulmonary	23 5
Renal	14 4
Splenic	8 8
Cerebral	7 7
Peripheral arteries	5 5
Mesenteric	1 9
Carotid or aortic	0 5

Mural thrombosis is found at necropsy in 44 per cent of all fatal cases of cardiac infarction and is presumed to be the source of the peripheral vascular lesions the fact that these lesions have been found in 46 per cent of cases with mural thrombosis (Wang Bland and White 1948) and in 39 per cent of cases without mural thrombosis does not invalidate this view for fresh intraventricular clots may be dislodged and leave no evidence of their origin On the other hand pulmonary embolism is nearly always attributable to phlebothrombosis in the legs not to right ventricular mural thrombosis and cerebral vascular lesions may certainly result from coincidental local thrombosis (Bean 1938)

Cardiac rupture occurs in 1 5 to 3 per cent or in 5 to 10 per cent of fatal cases (Oblath Levinson and Griffith 1952) usually within the first four days of the illness and chiefly in the older patients (Gans 1951) it is not necessarily a dramatic event for the perforation may be small and the signs and symptoms often those of cardiac compression from hæmopericardium rather than sudden catastrophe such cases sometimes living a week or more *Perforation of the interventricular septum* is seen occasionally and gives rise to the sudden development of a coarse systolic thrill and murmur in the third and fourth intercostal spaces towards the sternum (Fowler and Failey 1948) Heart failure has ensued rapidly in most of the cases reported (e g Leonard and Daniels 1938) Although the perforation may look small at necropsy and the track tortuous the shunt during life may be considerable as has been proved (inadvisedly) by means of cardiac catheterisation More than half the cases have died within the month

Rupture of one of the papillary muscles is a rare complication of cardiac infarction and results in the sudden development of severe mitral incompetence with secondary acute and intractable left ventricular failure usually ending in death (Craddock and Mahe 1953)

Left ventricular aneurysm may be found at necropsy in as many as 22 per cent of fatal cases (Wartman and Hellerstein 1948) but is recognised clinically in less than half of them In the series referred to above 25 were anterior and 10 posterior five of them ruptured The condition arises early and may be well developed by the time the patient is allowed up for fluoroscopy The X ray appearances have already been described (page 738) Clinically it is suggested by an unusual pulsation in the region of the apex beat when left ventricular enlargement is improbable on other grounds Scherf and Brooks (1949) described an odd high pitched gushing soft diastolic murmur over the aneurysm in three of their cases but this is unusual The electrocardiogram usually shows a monophasic Q wave and conspicuous and rather persistent elevation of the Q T segment over the aneurysm while the main QRS deflection is often upright in lead V_R (Goldberger and Schwartz 1948) (fig 15 25) If rupture does not occur during the first few weeks the prognosis is little if at all influenced by the aneurysm (Mover and Hiller 1951)

Fig 15 25 Monophasic Q waves and persistent elevation of the S T segment in all chest leads in a case of left ventricular aneurysm

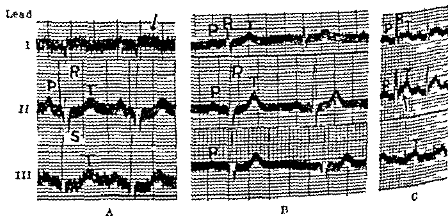


Fig 15 26 —Cardiac infarction complicated by perforation and hæmopericardium.

A Original anterior cardiac infarction

B After recovery

C After perforation of infarct (hæmopericardium)

Pericarditis may be of three kinds (1) a transient friction rub may be heard over an anterior apical infarct and represents a local pericardial reaction (2) there may be widespread pericarditis with friction heard at all areas or at a distance from the lesion which may complicate either anterior or posterior infarcts (3) there may be hæmopericardium resulting from ventricular perforation Local pericarditis does not alter the electro cardiographic pattern of infarction but widespread pericarditis may do so and hæmopericardium invariably does (fig 15 26) Pericardial friction of one kind or another is heard in about 10 per cent of cases

After effects The subsequent course is determined by the effect of the occlusion on the total coronary circulation and the amount of healthy muscle left Angina pectoris may develop or if it was present before it may be worse on the other hand if previous pain was due to local ischæmia at the site of the recent infarct angina may improve or temporarily disappear Left ventricular or congestive heart failure may develop during convalescence or subsequently and may cause the disappearance of angina Later cardiac rupture is rare and usually denotes fresh coronary occlusion Less than 10 per cent of ruptured hearts are due to an old ventricular aneurysm (Munck 1946)

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of myocardial infarction, many conditions must be borne in mind the most confusing are massive pulmonary embolism acute pericarditis dissecting aneurysm of the aorta diaphrag matic hernia œsophageal or gastric dysfunction and acute pancreatitis but diaphragmatic pleurisy especially when bilateral disease of the gall bladder perforated duodenal ulcer epidemic myalgia and pain referred from the spine may give rise to difficulty In *pulmonary embolism* the most important clue is early engorgement of the cervical veins and immediate hypotension whilst rhythm changes are very rare otherwise both symp toms and signs may be indistinguishable from those of coronary throm bosis and even limb lead electrocardiograms may resemble those of posterior cardiac infarction—Fortunately however chest lead graphs are diagnostic (page 813) *Acute pericarditis* may simulate cardiac infarction closely but may be distinguished by the electrocardiogram (page 658) *Dissecting aneurysm* is characterised by radiation of pain to the back and downwards by hypertension by the absence of electrocardiographic change by the development of aortic incompetence and perhaps by signs of involvement of carotid subclavian renal or femoral arteries (page 924) *Diaphragmatic hernia* should be considered when there are no changes in temperature white count E S R and electrocardiogram and may be diagnosed by means of a barium meal with the patient in the head down position *Œsophageal or gastric pain* may be felt in the centre of the chest and may resemble the pain of cardiac infarction but physical examinati

is entirely negative the electrocardiogram remains normal and the subsequent course is benign *Acute pancreatitis* may be recognised by the urinary diastase test

TREATMENT

Patients should be confined to bed at once and should remain there for three to six weeks or longer according to the severity of the illness and to the behaviour of the sedimentation rate and electrocardiogram If the blood pressure is low and the patient faint or dizzy he may have to lie flat otherwise and particularly if there is any sign of failure he should be propped up against a back rest in order to reduce the work of the heart

Semi starvation for the first few days followed by an 800 calorie diet during the dangerous period practically halves the mortality rate (Master *et al* 1936) Fruit drinks and soft stewed or fresh fruit with sugar and a little milk is all that should be allowed for the first forty eight hours The quality of the later light diet matters less than its bulk and calorific value but should contain little sodium if there is any evidence of failure and little fat

The most beneficial drug in the acute phase is *morphine* which should be given in adequate doses and as often as required to relieve pain and distress and to induce rest and sleep Excellent results are obtained when pain is severe by giving it intravenously in a dose not exceeding ¼ of a grain (15 mg) dissolved in at least 2 ml of sterile water or saline and at a slow rate three minutes being taken over the injection *Pethidine* 50 to 100 mg by mouth may be taken subsequently at four to six hourly intervals if necessary

Quinidine 3 to 5 grains (0 25 G) t d s has been given in the hope of preventing ventricular fibrillation and other changes of rhythm but with little success (Cutts and Rapoport 1952) although it prevents ventricular fibrillation in dogs (Wegria and Nickerson 1943)

Heparin and certain prothrombin inhibitors such as dicoumarol tromexan (ethyl biscoumacetate) and dindevan (phenylindanedione) have been used widely in recent years to prevent extension of coronary thrombosis mural thrombosis and phlebothrombosis

Heparin 15 000 units should be given intravenously at once followed by 15 000 units intramuscularly or subcutaneously eight hourly during the first two days Dindevan should also be given as soon as possible starting with 150 mg on the first day 100 mg on the second and 50 mg on the morning of the third subsequent doses being regulated according to the prothrombin time which should be maintained at two and a half times the prothrombin time in a normal control i e at a ratio of 2 5 The treatment should be started at once in the patient s home for laboratory control is unnecessary until the third day

The results of such treatment in 432 cases were compared with those of conservative management in 368 controls by a special committee of the American Heart Association and were reported by Wright Marple and Beck (1948) The chief findings were as follows

	Controls per cent	*Cases treated with anticoagulants per cent*
Mortality	24	15
Thrombo embolic deaths	10	3
Thrombo embolic complications	25	11

Very similar figures for 301 cases treated with anticoagulants and 160 controls were published by Kerwin (1953) in the treated group the mortality was 17 9 per cent and the incidence of thrombo embolic complications 7 6 per cent in the control series the mortality was 29 4 per cent and the incidence of thrombo embolic complications 20 per cent In Great Britain the results of anticoagulant therapy have been much the same Gilchrist and Tulloch (1954) for instance treated 321 cases over a period of seven years and claimed to have halved the mortality rate

Considering the uniformity of published results of anticoagulant therapy it is remarkable that many critical observers still feel uneasy about their reliability (e g Evans 1954) The difficulty in accepting the figures arises from the disbelief that drugs like dicoumarol tromexan and dindevan could diminish the mortality from ventricular fibrillation shock cardiac rupture and heart failure which together should be responsible for the great majority of deaths Prior to anticoagulant treatment deaths from pulmonary and systemic embolism were put no higher than 5 per cent so that allowing for a five fold decrease in thrombo embolic mortality (Wright Marple and Beck 1954) it is still difficult to see why the total death rate should fall more than 4 per cent It is possible however that extension of coronary thrombosis is a more important cause of disaster than at present believed and that anticoagulants tend to prevent this Of 95 deaths from cardiac infarction analysed by Selzer (1948) for instance five were attributed to secondary coronary thrombosis Both heparin and dicoumarol also appear to be coronary vasodilators (Gilbert and Nalefski 1949) and may therefore improve the total coronary flow

According to Schnur (1953) and Russek and Zohman (1954) the risk of serious hæmorrhage (1 per cent) does not justify the use of anticoagulants in mild cases for in these the natural mortality is only 3 per cent, and the frequency of thrombo embolism 0 8 per cent By mild is meant a first attack absence of shock disappearance of severe pain within a few hours normal rhythm absence of heart failure absence of gallop rhythm no cardiac enlargement and no diabetes Against this attitude may be set

negligible risk of hæmorrhage when dindevan is used and when good laboratory facilities are available, and the disastrous consequences that may follow extension of the thrombosis

Permanent anticoagulant treatment to prevent further attack of coronary thrombosis is under trial (Nichol and Borg 1950) An encouraging report comes from Suzman Ruskin and Goldberg (1955) who treated 82 cases continuously over periods ranging between three month and six years Comparing the results with those of 88 untreated control observed over the same period they found the mortality was reduced from 33 to 7 3 per cent and the frequency of recurrences of coronary thrombosis from 24 to 7 per cent When severe cases only were considered (67 cases) the mortality was still only 9 per cent in the treated group, compared with 46 7 per cent in 60 untreated controls and the frequency of recurrences 7 per cent against 21 per cent in the controls Owren (1954) treated 128 cases of uncomplicated angina pectoris with dicoumarol or dindevan for one to five years coronary thrombosis occurred in ten instances during this period and the mortality during the first year of treatment was 5 per cent of 108 patients who had had one previous attack of cardiac infarction seven developed a second coronary thrombosis during the same one to five year period of anticoagulent treatment These results compare favourably with the natural course of ischæmic heart disease

The *coronary vasodilators* with the possible exception of aminophylline do not relieve the pain of cardiac infarction and do not influence its course aminophylline may perhaps improve the collateral circulation and may help to prevent cardiac asthma

Oxygen may be given in severe cases but is not routine therapy in Great Britain There may be some advantage in supersaturating the arterial blood particularly when respiration is depressed spontaneously or as a result of morphine

Cortisone has been said to halve the mortality from experimental cardiac infarction in animals (Johnson *et al* 1953) moreover infarcts produced in the treated animals were found to be far smaller than in the control Healing however was delayed and fibroblastic proliferation much decreased Opdyke (1953) on the other hand found no diminution in the size of experimentally induced infarcts in cortisone treated animals

Treatment of complications

Shock has been treated actively in recent years and its mortality has been reduced from 80 to 50 per cent Blood transfusion was tried (Epstein and Relman 1949) but soon abandoned, and intra arterial infusion proved no better (Berman *et al* 1952) but encouraging results have been obtained with vasopressor drugs such as mephentermine noradrenaline and aramine

Mephentermine (wyamine) may be given intramuscularly in a dose of 30 to 40 mg, and repeated when necessary or intravenously at the rate

of 1 mg per minute until the blood pressure is 120 mm Hg which is usually reached in 5 to 20 minutes (Hellerstein Brofman and Caskey 1952)

Noradrenaline or L noradrenaline (levophed) 10 mg. dissolved in a litre of 5 per cent glucose solution may be given by intravenous drip infusion at the rate of 10 to 20 drops per minute each ml (15 drops) of the solution contains 10µg of noradrenaline The rate of infusion should be regulated to maintain the blood pressure at 120 mm Hg and continued as long as necessary (up to 72 hours) In England Shirley Smith and Guz (1953) reported encouraging results with this treatment In the United States Griffiths *et al* (1954) reduced the mortality of shocked cases from 80 to 47 8 per cent prior to the treatment 128 out of 161 shocked patients died in their series of 816 proved cases of acute coronary thrombosis since starting treatment with pressor amines 64 out of 134 shocked cases died and when treatment was begun within three hours of the onset only 13 per cent died These figures are impressive

Aramine in doses of 0 01 to 0 1 mg per kilo body weight improves cardiac function and coronary blood flow while maintaining the blood pressure in cardiogenic shock (Sarnoff *et al* 1954) It may be given orally intramuscularly or by drip infusion (0 1 to 0 5 mg per minute)

Since appreciating that shock in acute cardiac infarction is a form of acute heart failure it is rational to try digitalis Gorlin and Robin (1955) reported good results with lanatoside C or Ouabain intravenously in four cases although they used very small doses (0 4 mg of lanatoside C and 0 05 to 0 2 mg of Ouabain) This lead should be followed up

Conventional heart failure usually responds well to routine treatment with posture a low sodium diet mercurial diuretics and digitalis The danger of the digitalis glycosides (Travell Gold and Modell 1938) should not be over emphasised and they must not be withheld when the need for them arises

Serious disturbances of rhythm call for their standard treatment Ventricular tachycardia can usually be controlled with adequate doses of quinidine or procaine amide atrial fibrillation flutter or tachycardia with digitalis heart block with ephedrine Under the appropriate circumstances these drugs may have to be used boldly without fear that they may cause cardiac standstill or ventricular fibrillation in the presence of cardiac infarction

The frozen shoulder syndrome (left) that can prove troublesome for months after cardiac infarction may often be relieved by cortisone according to Russek *et al* (1953) Hydrocortisone 50 mg in a 2 ml suspension with the addition of 1 000 units of hyaluronidase and 2 ml of 2 per cent procaine may be injected weekly into the subacromial bursa anteriorly into the long head of the biceps antero laterally and into the joint capsule posteriorly as described by Crisp and Kendall (1955)

Subsequent management

If the course is benign and the patient looks and feels well, he may be allowed up after three weeks provided the sedimentation rate has returned to normal and the electrocardiogram does not show a large infarct Most cases require a month in bed and a further fortnight resting at home on a couch but those with complications should remain in bed for six weeks or longer

Six weeks to three months convalescence is usually needed while the patient regains his confidence and gradually resumes his ordinary activities Radical change of employment is rarely practicable in this age group but lighter work and less responsibility may have to be advised Relatively good recovery from the first attack is the rule but severe angina or recurrent congestive failure may cause total incapacity after second or third attacks

PROGNOSIS

With conservative treatment the mortality during the first month of acute cardiac infarction is 25 per cent This figure is based on 3 948 cases collected from ten unselected series in the literature mostly first attacks and does not take into account all those cases that failed to survive long enough to receive skilled medical attention and hospital care The mortality was also 25 per cent for 2 733 first attacks only for second and third attacks it is said to be higher Doscher and Poindexter (1950) found a combined mortality rate of 23 5 per cent in over 4 000 cases in the literature

When assessing the influence of any new therapy on the mortality rate of acute cardiac infarction many factors must be taken into consideration

1 First attacks are believed to have a lower mortality than subsequent attacks assuming (possibly without justification) that abrupt death at the onset is not more frequent in first attacks

2 Four fifths of all deaths from acute cardiac infarction occur in the first twenty four hours 60 per cent in the first two hours and 50 per cent within the first fifteen minutes at least in men under 40 years of age having their first attack (Yater *et al* 1948)

3 The mortality in women averages 50 per cent higher than in men (Mintz and Katz 1947 Doscher and Poindexter 1950)

4 Mortality in men is proportional to age in a group of 276 cases studied by Fitzgerald Peel (1955) it ranged from 5 per cent in men under 44 years old to 35 per cent in men over 65 in women it was 25 per cent at all ages

5 The following complications adversely influence the mortality which is given in brackets when known complete heart block (80–90 per cent) shock (75–80 per cent) paroxysmal tachycardia of any type or atrial flutter (66 per cent) pneumonia (57 per cent) left ventricular or congestive heart failure (50 per cent) gallop rhythm a pulse pressure under 20 mm Hg

a blood pressure under 90 mm Hg bundle branch block unquestionable cardiac enlargement intractable pain diabetes mellitus and marked obesity (Mintz and Katz 1947 Russek and Zohman 1952)

6 The following factors do not influence the mortality rate previous angina pectoris previous hypertension absence of pain the site of the infarct ectopic beats and pericarditis (Mintz and Katz 1947)

7 The mortality in favourable cases without any of the adverse features listed above is only 3 to 5 per cent and the incidence of thrombo embolism in this group is only 1 to 3 per cent (Russek and Zohman 1952 1954)

8 Particularly favourable are those cases with electrocardiograms that show simple inversion of the T wave only without pathological Q waves and without initial elevation of the RS T segment (East and Oram 1948 Papp and Smith 1951 Holzman 1955) especially when there is no significant fever leucocytosis or rise of sedimentation rate (Helander 1950)

Mortality of specially treated cases

With prompt skilled medical and nursing attention early intravenous heparin proper use of vasopressor drugs within three hours of the onset of shock a semi starvation diet (800 calories approximately) containing not more than 0 5 G of sodium for the first few days prothrombin inhibitors for four to six weeks either in all cases or at least in those with one or more unfavourable features early recognition and efficient treatment of left ventricular or congestive heart failure immediate antibiotic therapy for complicating pneumonia good control of diabetes mellitus and the intelligent treatment of serious changes of rhythm the natural mortality of 25 per cent in all cases that survive the first fifteen minutes of the attack should be reduced to about 10 per cent

Ultimate prognosis

Of patients who survive the first acute attack of cardiac infarction about a third make a complete functional recovery 50 per cent have angina pectoris or limited cardiac reserve but are able to lead useful lives and 20 per cent are seriously incapacitated with severe angina or heart failure (Mussafia and Masini 1948 Master and Jaffe 1951 Cole Singian and Katz 1954) If the ultimate prognosis of any particular case is to be based on statistical evidence these three groups must be considered separately

Patients with good functional recovery are not only free from angina pectoris but are also able to increase their cardiac output normally on effort (Chapman and Fraser 1954) About 90 per cent of such patients survive five years and 70 per cent ten years (Master and Jaffe 1951 Cole *et al* 1954)

Of the patients with mild or moderate angina pectoris about three quarters survive five years and one half survive ten years (Cole *et* 1954)

In the severe group, however the majority die within five years

The crude average life expectation following recovery from the first attack of cardiac infarction is about eight years The chief causes of death include fresh cardiac infarction (66 per cent) and heart failure (20 per cent) (Katz *et al*, 1949)

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CHAPTER XVI

HYPERTENSIVE HEART DISEASE

Hypertensive heart disease is but one facet of the whole problem of systemic hypertension It is necessary to consider this problem first

DEFINITION

Hypertension implies elevation of the basal blood pressure above the arbitrary normal limits of 145/90 mm Hg Physiological vasoconstriction or a transient increase of cardiac output due to emotion cold or other trivial cause is common and modifies the significance of casual high readings of the order of 160/90 mm Hg The basal pressure is that obtained when the subject is lying down and when successive readings at five minute intervals have dropped to a steady level If there were an easy bedside method of measuring the cardiac output hypertension would be expressed in terms of total peripheral resistance In healthy young adults

$$R \text{ (resistance)} = \frac{80 \text{ to } 100 \text{ mm Hg (mean arterial pressure)}}{5 \text{ to } 8 \text{ L/min (cardiac output)}}$$
$$= 10 \text{ to } 20 \text{ units}$$
$$= 800 \text{ to } 1\,600 \text{ dynes sec/cm}^5 \text{ (page 177)}$$

Unquestionable hypertension means a peripheral resistance above 25 units (2 000 dynes sec/cm ^{5}) It is insufficiently realised that with an average peripheral resistance of 15 units a cardiac output of 10 litres per minute which is common in mildly excited young adults would raise the blood pressure to around 210/110 mm Hg (mean 150 mm Hg) With a relatively high normal resistance of 18 units and a cardiac output of 12 litres per minute resulting from more marked excitement (also common enough) the physiology of the circulation could still be normal with a blood pressure of 300/150 mm Hg (mean 210) That such hyperkinetic levels are not commonly encountered in healthy but apprehensive young adults is due to the fact that when the cardiac output rises in response to adrenergic stimuli the peripheral resistance falls The figures given however should serve to emphasise the fact that measurement of the blood pressure without reference to the cardiac output provides no evidence of the state of vasomotor tone and is therefore a poor method of detecting essential hypertension or of estimating its degree Once this is understood many of the anomalies that surround the height of the blood pressure in normal hypertensive subjects fall into line *Hyperkinetic elevation of the pressure is not essential hypertension*

When elevation of the blood pressure shows disproportion between systolic and diastolic levels, systolic bias favours rigidity of the aorta and large vessels as in atherosclerosis or increased force of cardiac contraction as in thyrotoxicosis whereas diastolic bias favours vasoconstriction, as in true hypertension

VARIETIES OF HYPERTENSION

Hypertension may be paroxysmal, as in phæochromocytoma of the adrenal medulla transient, as in acute nephritis and toxæmia of pregnancy or persistent, as in chronic nephritis chronic pyelonephritis surgical kidney coarctation of the aorta Cushing s syndrome and essential and malignant hypertension High blood pressure accompanying thyrotoxicosis and the climacteric is coincidental statistical analysis shows no significant *correlation* and the *pressure does not fall when these disorders* are corrected (Bechgaard 1946) The blood pressure in obese subjects may appear to be higher than it really is owing to the unreliability of the cuff method of measurement when applied to a fat limb lower pressures may be recorded by direct arterial puncture Under certain conditions eg during a rigor when there is intense vasoconstriction or when the main artery to the limb is partly occluded, the blood pressure reading may be *much lower when measured by the cuff method than* when measured by direct arterial puncture indeed it may be immeasurable by ordinary means when direct puncture proves it to be in the region of 100 mm Hg *Such fallacies* must be constantly borne in mind *Hypertension associated with* mitral stenosis is almost certainly a matter of chance apart from the transient rise of pressure that may result from heart failure

INCIDENCE

In 1928 hypertension accounted for 14 8 per cent (Bell and Clawson) to 20 per cent (Fahr) of all deaths in the U S A in people over 50 years of age In England and Wales the Registrar General s Statistical Review for 1953 reveals that 4 per cent of all deaths (8 per cent of cardiovascular deaths) were due to hypertension and another 13 5 per cent of all deaths (27 per cent of cardiovascular deaths) *to stroke chiefly cerebral hæmorrhage or thrombosis*

If a blood pressure of 150/100 mm Hg or above means hypertension then the prevalence of this disease is 5 per cent *in young adults* 10 to 20 per cent in the fifth decade 20 to 30 per cent in the sixth decade and 35 to 40 per cent in those between the ages of 60 and 65 (Master *et al* 1952) As pointed out by Hamilton *et al* (1954) there *is no sharp dividing* line between what is normal and what is abnormal If 180/105 mm Hg is accepted as the lower limit of genuine hypertensive disease then its prevalence is 0 7 per cent in young adults under 40 years of age 3 per cent *in the fourth decade 6 per cent in the fifth decade* and 10 per cent between the ages of 60 and 65 (Master *et al* 1952) Males are more prone to

hypertension than females up to the age of 40, but thereafter it is the other way about

At least 80 per cent of hypertensive subjects are between 40 and 70 years of age the peak period being 50 to 59 (Janeway 1913 Bechgaard 1946) According to Platt (1948) severe persistent hypertension in persons under 40 years of age is commonly renal less than a third of his series were essential and he encountered no primary malignant cases under the age of 34

The sex incidence is about equal men being rather more frequently affected in the upper classes (Janeway 1913 Ehrstrom 1918) women in the lower (Blackford *et al* 1930 Bechgaard 1946) Malignant hyper tension however affects three men to one woman

About 80 to 85 per cent of cases of persistent hypertension are essential about 2 per cent are primary malignant and most of the remainder are renal Brod (1955) found a particularly high incidence of malignant hyper tension amongst his cases of chronic pyelonephritis (20 per cent)

High blood pressure appears to be linked with civilisation it is said to be rare or uncommon in China amongst orientals generally (Harris 1927) and in negroes (Donnison 1929) but it is as common or more common in civilised negroes in the U S A as in the white population (Fishberg 1939) The evidence has been reviewed by Smirk (1949)

PATHOGENESIS

Paroxysmal hypertension is due to an excess of circulating adrenaline released by a phæochromocytoma of the adrenal medulla (Beer King and Prinzmetal 1937) it is now known that there is also an excess of nor adrenaline sometimes one and sometimes the other predominating (Pitcairn and Youmans 1950)

Transient hypertension in acute nephritis appears to depend upon a ner vous rather than a humoral agent (Pickering 1943) and may be due to extra renal factors (Kylin 1926) There is reason to believe that acute nephritis is an allergic vascular reaction to the products of remote bacterial infection (Cavelti and Cavelti 1945) usually but not exclusively strepto coccal the brunt of the attack falling on the glomerular tufts but the capillaries elsewhere not escaping entirely General vasospasm may cause the hypertension Wilson (1953) on the other hand accepts the obvious and assumes that the hypertension of acute nephritis is renal and humoral in origin

Hypertension in *toxæmia of pregnancy* may be transient and behave like that in acute nephritis or it may be persistent and resemble essential or malignant hypertension (Golden Dexter and Weiss 1943) Since the blood volume and cardiac output are raised the hypertension may be partly hyperkinetic More measurements of the peripheral resistance in toxæmia of pregnancy are needed

High blood pressure in *coarctation of the aorta* (page 332) probabl

results from diminution of the renal blood flow It does not occur experimentally if the aorta is constricted below the origin of the renal arteries (Rytand 1938)

Hypertension resulting from *chronic nephritis, chronic pyelonephritis* (Schoen 1930 Longcope and Winkenwerder 1933) and certain *surgical kidneys* (Braasch Walters and Hammer 1940) is almost certainly attributable to a humoral agent liberated by the diseased kidney (Pickering 1943) at least in the first instance

Malignant hypertension may develop in any form of hypertension provided the diastolic blood pressure rises sufficiently particularly when it does so rapidly (Pickering 1952)

ETIOLOGY OF ESSENTIAL HYPERTENSION

Certain predisposing factors must be considered first

Heredity According to Platt (1947) *essential hypertension could be a* hereditary disease conveyed as a Mendelian dominant with a rate of expression of more than 90 per cent This may be an extreme view but the importance of the hereditary factor cannot be denied Thus Ayman (1934) studying 277 families found hypertension in the children in 3 1 per cent of the families when both parents were normal in 28 3 per cent when one parent was hypertensive and in 45 5 per cent when both parents were hypertensive Again *in an investigation based upon 256 members of 50* families Hines (1940) found that the children were hyper reactors to the cold pressor test in 43 4 per cent when one parent was either hypertensive or a hyper reactor and in 95 per cent when both parents were affected In Bechgaard s series of over 1 000 cases of persistent hypertension which included 20 7 per cent possible renal cases *(in which there* is no hereditary factor) one or both parents were seriously hypertensive in 75 per cent

Hyper reaction to pressor agents The excessive reaction of hypertensive subjects to the cold pressor test of Hines (1940) is the best example The test is carried out as follows the basal blood pressure is first recorded in the usual way the subject s free hand is then plunged into ice cold water *(3° to 5 C) to just above the level of the wrist* and immersed for one minute while the blood pressure is recorded at half minute intervals In 85 per cent of normal persons the blood pressure rises an average of 12 4/10 1 mm Hg and returns to its previous level within two minutes If the immersed limb is anæsthetic there is no response whether the anæsthetic is organic or hysterical (Wolff 1951) A rise of more than 20/15 mm Hg is regarded as a hyper reaction Patients with established essential hypertension show an average rise of 46 6/30 9 mm Hg 95 per cent being hyper reactors Follow up studies indicate that apparently normal individuals who are hyper sensitive to the cold pressor test are likely to develop persistent hypertension Hines also claims that high casual readings due to emotion have the same significance and Harris *et al* (1953)

agree but this is not substantiated by the subsequent histories of patients with Da Costa's syndrome (Grant 1925 Wood 1941)

Holding the breath for 20 seconds may also be used as a pressor agent in much the same way, and compares favourably with the cold pressor test (Ayman and Goldshine 1939)

Other factors The influence of civilisation and of sex in malignant hypertension have already been mentioned

Structural changes in the vessels Certain structural vascular changes often found associated with hypertension have been proved to play no part in its production. Atherosclerosis is innocent in this respect unless a plaque constricts the renal artery increased rigidity of the aorta and great vessels may raise the systolic pressure increase the pulse volume and accelerate the speed of the pulse wave but it has little influence upon the mean blood pressure Calcification of the media of medium sized arteries has a similar effect The characteristic vascular lesion which is the signature of malignant hypertension necrosing afferent glomerular arteriolitis is a result not a cause of extreme hypertension Multiplication of the internal elastic lamina and hypertrophy of the media of small arteries and arterioles are also effects not causes of sustained hypertension. Hyaline thickening of the intima especially of the afferent glomerular arteriole found in 98 per cent of cases of essential hypertension is the only vascular lesion possibly to blame which has not yet been proved to be a result of high blood pressure (Pickering 1943)

Experimental studies The classical experiments of Goldblatt (1934 *et seq*) proved that persistent hypertension could be induced in dogs by constricting both renal arteries unilateral constriction failed unless the other kidney was removed Hypertensive retinopathy and widespread arteriolar necrosis similar to malignant hypertension in man were reproduced by more severe constriction but the renal vessels distal to the clamp were spared Similar results were obtained in rabbits by Wilson and Pickering (1937) In 1939 Wilson and Byrom succeeded in causing persistent hypertension benign or malignant, in rats by constricting only one renal artery The vessels in the other kidney then showed changes comparable in all respects to those seen in benign or malignant hypertension in man

The conclusion that the difference between essential and malignant hypertension is merely one of degree is supported by the occasional development of malignant changes in practically all varieties of hypertension including paroxysmal, transient and renal hypertension moreover in the early malignant stage renal biopsy usually reveals no evidence of arteriolar necrosis indicating that this is not an essential part of the picture, but merely a late consequence (Castleman and Smithwick 1943)

Biochemical hypothesis concerning the cause of hypertension Experimental hypertension of the kind just described is believed to depend upon the liberation of an excess of renin by the ischaemic kidney Renin combines with an enzyme hypertensinogen which is a normal constituent of the

plasma globulins, to form a pressor substance hypertensin or angiotonin (*Braun Menendez et al* 1939) *Hypertensin is said to be destroyed by* another enzyme hypertensinase (Pickering 1943)

There is as yet, no direct proof that essential hypertension in man is caused by this mechanism although it seems to explain renal hypertension It may also explain rare cases of hypertension associated with atherosclerotic obstruction of one or both renal arteries (Yuile 1944) It should be noted that unilateral renal disease is capable of causing hypertension in man, in other words man behaves like the rat in this respect, not like the dog or rabbit

Physiology of the circulation in essential hypertension In essential hypertension vasoconstriction affects chiefly the efferent glomerular arterioles of the kidney the intraglomerular pressure being raised and the cortical *blood flow diminished, obviously if the latter were due to* vasoconstriction proximal to the glomeruli the intraglomerular pressure would be lowered Blood appears to be diverted from the renal cortex into other channels The classical studies of Trueta and his colleagues (1947) make it highly probable that the juxta medullary by pass provides the principal diversion The vessels of the skin and brain are constricted more or less sufficiently to *prevent an increased blood flow through* these territories on the other hand the arterioles in skeletal muscle and probably in the heart are little if at all constricted so that they may passively yield to the raised pressure and take some of the shunt The behaviour of the splanchnic vessels remains to be investigated but in normal subjects their reactions tend to be opposite to those in the skin (Grayson 1950) The cardiac output blood volume and blood viscosity are normal Vasoconstriction appears to be humoral rather than nervous in mechanism (Pickering 1945) Hypertensin causes a similar type of vasoconstriction the chief effect is on the efferent glomerular arterioles the skin is involved only to the extent of preventing secondary increase of blood flow the skeletal muscles take some of the shunt That hypertensin is the humoral cause of essential hypertension is therefore an attractive hypothesis (Pickering remarks that the brain and heart being two of the most important organs in the body are provided with special pressor mechanisms the carotid sinus and aortic arch which respond to falling intravascular pressure by causing vasoconstriction as the nature of these organs demands that appropriate adjustments are immediately executed it is natural that the mechanism of this vasoconstriction is nervous But the kidneys are just as vital and it would therefore harmonise with general principles if they too were provided with a pressor mechanism to ensure adequate intraglomerular pressure without which filtration would cease but there is no necessity for sudden adjustments but rather for prolonged ones A humoral mechanism would meet the requirements nicely)

Nevertheless as previously stated proof that essential hypertension in man is due to excessive liberation of renin is lacking Transfusion experi

ments have failed to demonstrate a pressor agent in the venous blood of hypertensive subjects and Light and I (1939) failed to demonstrate a pressor agent in a pint of blood taken from the renal vein of a patient with malignant hypertension and transfused into a boy of nine Even if the humoral mechanism were proved to be the renin hypertensin system we should still be ignorant of the cause of its hyperactivity

A promising line of investigation seems to be that opened up by Trueta and his colleagues at Oxford They have shown that blood reaching the kidney has two alternative routes (1) through the glomeruli of the cortex (2) through a juxta medullary by pass Blood may be diverted from the cortex in varying degree as a result of emotion shock crushing injuries hæmorrhages certain drugs certain bacterial toxins and probably by innumerable other agents In cases of Bright s disease they have noticed degenerative changes in the juxta medullary glomeruli consistent with constant operation of the shunt The significance of these findings will not be overlooked particularly their suggestion that the juxta medullary by pass may act as a functional Goldblatt clamp

It is possible that the cause of essential hypertension is simply physiological hypertension repeated too often or sustained for too long a period, as suggested by Smirk (1949) Whether repetitive physiological hyper tension is chiefly hyperkinetic neurogenic (vasoconstrictive) or humoral (vasoconstrictive) is immaterial to this hypothesis which holds that a raised blood pressure however produced may initiate secondary reactions which themselves increase the total peripheral resistance and so perpetuate the hypertension Agents capable of causing sufficiently repetitive or prolonged hypertension to excite these secondary changes include a par ticular type of personality that over reacts to stress (hereditary factor) prolonged emotional strain (psychological factor) acute nephritis tox æmia of pregnancy paroxysmal hypertension from phæochromocytoma and certain hyperkinetic circulatory states such as thyrotoxicosis Second ary changes that may perpetuate the hypertension are renal ischæmia and arteriosclerosis in its broadest sense, but a more important unknown factor is postulated A similar hypothesis has been put forward to explain pul monary hypertension for sustained pulmonary vasoconstriction also seems to result from pulmonary hypertension *however caused* (page 839)

CLINICAL FEATURES

PAROXYSMAL HYPERTENSION

Paroxysmal hypertension first described by Frankel (1886) is rare being responsible for only 0 5 per cent of cases of severe persistent hyper tension (Graham 1951) It usually occurs in youthful or early middle aged subjects of either sex and is characterised by recurrent attacks of pal pitation headache and vomiting angina pectoris or even acute pulmonary œdema (Howard and Barker 1937) may be associated Abdominal com

pression as occurs on stooping may provoke an attack but usually there is no previous precipitating cause During the crisis, which may last for minutes or hours, the blood pressure (systolic and diastolic) is extremely high most of the skin is cold, pale and mottled but the forehead, face and neck may be flushed Sweating and trembling may follow Between attacks the patient is usually well but persistent hypertension occasionally malignant, develops sooner or later in the majority (Green 1946)

The quality of the symptoms depends upon whether the tumour liberates chiefly adrenaline or noradrenaline although both are usually present in excess Adrenaline is the body s emergency hormone and is normally released by the suprarenal medulla in amounts proportional to physiological estimates (Cannon 1940) It increases the heart rate venous pressure (Iglauer and Altschule 1940) and strength of cardiac contraction (Marsh *et al* 1948) so that the cardiac output is increased by means of all three reserve mechanisms (McMichael and Sharpey Schafer 1944 *Goldenberg et al* 1948) *while the coronary blood flow is* augmented (Anrep and Stacey 1927) and the total peripheral resistance diminished (von Euler and Liljestrand 1927) Although the blood flow through the skin (Barcroft and Swan 1953) and through the kidneys (Barclay Cooke and Kenney 1947) is reduced the blood flow through skeletal muscle (Allen Barcroft and Edholm 1946) and liver (Bearn Billing and Sherlock 1952) is greatly increased Adrenaline also stimulates all impulse forming foci in the heart whether normal or abnormal The chief clinical effects of an excess of circulating adrenaline are therefore pallor of the skin tachycardia abnormalities of rhythm a bounding pulse marked elevation of the systolic but less of the diastolic blood pressure (hyperkinetic hypertension) and a hyperdynamic heart action the chief symptoms are palpitations and a sense of alarm

Noradrenaline is liberated physiologically at sympathetic nerve endings where it activates effector cells (von Euler 1946 1948) but it is also found in the adrenal medulla where it forms up to 25 per cent of the total secretion (Swan 1952) Noradrenaline is a powerful vasoconstrictor of all but the coronary vessels and causes a sharp rise of systolic and diastolic blood pressures and of total peripheral resistance The pulse rate slows reflexly owing to stimulation of carotid and aortic baroreceptors and though the stroke volume and power of ventricular contraction may be enhanced the minute output does not rise (Goldenberg *et al* 1948) Noradrenaline does not stimulate impulse forming foci in the heart and does not encourage changes of rhythm (Nathanson and Miller 195) The chief clinical effects of an excess of circulating noradrenaline are therefore pallor, systolic and diastolic hypertension, and bradycardia

Mixtures of adrenaline and noradrenaline (arterenol) infused at the rate of 10 µg per minute behave like adrenaline when there is less than 25 per cent of noradrenaline in the mixture (as in normal medullary secretion) with adrenaline/noradrenaline ratios of 3/1 to 1/3 the adrenaline effec

still predominate but with ratios of 1/8 or less the noradrenaline effects predominate balanced effects are observed with ratios between 1/3 and 1/8 (De Largy *et al* 1950)

A mass about the size of an orange may be felt in the abdomen in one third of the cases or may be demonstrated by simple skiagrams pyelograms or other radiological methods. The adrenal medullary tumour is commonly unilateral and benign There is usually a considerable excess of circulating adrenaline or nor adrenaline all the time and in attacks there may be a thousand times the normal quantity (Mackeith 1944) The electrocardiogram may show the usual pattern associated with persistent hypertension or it may show evidence of acute left ventricular stress during attacks—inversion of the T wave in leads facing the surface of the left ventricle

Death may result from cerebral hæmorrhage acute pulmonary œdema or ventricular fibrillation

Following the demonstration by Clerc and Sterne (1937) that a synthetic benzodioxan (diethyl aminoethyl benzodioxan) in oral doses of 0 05 G six hourly relieved all symptoms immediately and prevented further attacks the administration of this substance has been used as a diagnostic test for the condition (Goldenberg *et al* 1947 Cahill 1948) The usual dose is 0 25 mg per kilogram body weight intravenously In cases of phæochromocytoma the systolic and diastolic blood pressures drop sharply for 10 to 15 minutes whereas in other forms of hypertension they tend to rise a little sometimes alarmingly so

Of the newer adrenolytic drugs such as dibenamine (3 to 5 mg /Kg intravenously) dibenyline or dibenzyline (0 25 to 0 5 mg /Kg intravenously or 20 to 50 mg three or four times daily orally) rogitine (*vide infra*) and ilidar (25 to 50 mg three or four times daily by mouth) rogitine is probably the most satisfactory for detecting or excluding phæochromocytoma Rogitine (phentolamine) is related to priscoline both being derivatives of amidazoline For diagnostic purposes a dose of 5 mg is given intravenously in cases of phæochromocytoma the blood pressure falls more than 35/25 mm Hg within two or three minutes and then gradually returns to the basal level over the next 10 to 15 minutes (Gifford Roth and Kvale 1952) Dangerous pressor reactions in essential or malignant hypertension, such as may occur with benzodioxane (Rosenheim, 1954) do not seem to occur with phentolamine The drug may also be given orally in doses of 20 mg three or four times daily

A marked fall of blood pressure after intravenous dibenamine dibenzyline or ilidar is not specific for phæochromocytoma for these drugs are all sympatholytic as well as adrenolytic in the doses used whereas phentolamine is not

The intravenous injection of 0 025 mg of histamine (Roth and Kvale 1945) or of 300 mg of tetraethylammonium bromide is also helpful in diagnosis for in cases of phæochromocytoma both raise the pressure

(La Due *et al* 1948) Mecholyl may have the same effect but is unreliable (Anderson *et al*, 1952) Hexamethonium (and presumably ansolysen) appears to excite similar responses to those of tetraethyl ammonium (Freis *et al* 1951)

The most reliable test for phæochromocytoma however is to estimate the plasma adrenaline and noradrenaline or the output of these catechol amines in the urine In normal controls and in patients with essential hypertension they should not exceed 2 5 μg per litre in the plasma (mean 1 6), mostly noradrenaline whereas in cases of phæochromocytoma with sustained hypertension and in paroxysmal cases after a test dose of histamine they usually exceed 12 μg per litre adrenaline alone exceeding 4 μg (Manger *et al* 1954) In normal subjects at rest in bed only infinitesimal amounts of adrenaline and noradrenaline are excreted and in subjects leading quiet lives only about 5 μg of adrenaline and 20 to 40 μg of noradrenaline are excreted within 24 hours In cases of phæochromocytoma however up to 100 times this quantity is excreted within 24 hours (Engel and von Euler 1950)

Treatment is surgical and may be entirely successful but the operative mortality is about 30 per cent (Mackeith 1944) The chief dangers are extreme hyper-adrenalism during manipulation of the tumour and a profound drop in blood pressure following its removal Dibenyline 20 mg three or four times daily (Allen *et al* 1951) or phentolamine, 20 to 40 mg t d s may be given orally to control the pre operative situation and noradrenaline may be infused post operatively, at a rate of approximately 10 μg per minute to control the transient circulatory collapse that may follow removal of the tumour

TRANSIENT HYPERTENSION

The clinical features of acute nephritis and toxæmia of pregnancy are beyond the scope of this work and their effect upon the heart is discussed elsewhere (page 638)

PERSISTENT HYPERTENSION

It is doubtful whether any symptoms can be ascribed to high blood pressure itself Certainly the majority of cases are discovered accidentally or by reason of complications Headaches fatigue dizziness difficulty in concentration and palpitations are commonly due to anxiety whether the blood pressure is raised or not Redistribution of blood due to selective vasoconstriction may however determine the behaviour of two variables It was stated previously that vasoconstriction in skin and brain was more or less sufficient to prevent an increase of blood flow through these territories as a result of raised pressure the words more or less may now be amplified Thus more cutaneous vasoconstriction may be responsible for the pale hypertensive less for the red more cerebral vasoconstriction may be responsible for dizziness failing memory and for general mental

deterioration less for headache The more important symptoms associated with hypertension are due to cardiac renal or cerebral complications and will be discussed later

The blood pressure is necessarily raised a diagnosis of previous persistent hypertension when the blood pressure is found to be normal is nearly always wrong unless there is severe hæmorrhage shock massive pulmonary embolism or myocardial infarction It is customary to recognise four grades of hypertension according to the level of the diastolic pressure between 95 and 110 mm Hg is considered mild 110 to 125 moderate 125 to 140 severe, above 140 gross The systolic pressure may be at any level between 150 and 300 mm Hg and may modify the grade accordingly With mild hypertension it is usually between 150 and 200 with moderate hypertension between 180 and 230 with severe between 210 and 260 with gross between 240 and 300 Essential and nephritic hypertension may be of any grade malignant hypertension is always severe or gross The frequent discrepancy between the grade of hypertension itself and the severity of the disease as a whole is explained by the fact that the blood pressure without reference to the cardiac output is only a rough guide to the total peripheral resistance

The pulse is firm and varies considerably in amplitude from case to case In the more severe grades it is apt to be small in those with marked atherosclerosis large If the pulse is full and bounding the raised pressure is more likely to be due to a hyperkinetic circulatory state (high cardiac output) Hard tortuous or calcified peripheral arteries indicate atherosclerosis or Monckeberg s sclerosis not hypertension—although they may be associated In the latter event one or other carotid usually the right may be kinked and then mistaken for an aneurysm or carotid pulsation may be so increased in amplitude as to suggest aortic incompetence A diminished and delayed femoral pulse associated with absent dorsalis pedis and posterior tibial pulses indicates coarctation of the aorta Pulsus alternans may occur in severe cases and is usually associated with heart failure or with ectopic beats

Retinoscopy may reveal arterial thickening hæmorrhages exudates or papillœdema (Liebrecht 1859) and should never be omitted There are five signs of arterial thickening (1) increased tortuosity (2) notching pinching or S shaped bending of veins at arterio venous crossings (3) uniform or irregular narrowing of the arterial blood streams owing to reduction in the diameter of the vascular lumina (4) white arterial fringes or thin white lines bordering the red arterial streams representing the thickened white walls of the arteries themselves—they are rarely seen in more than one or two places and then only for a short distance usually on a bend (5) the single white streak, representing a thrombosed artery with an obliterated lumen Occasionally the distal part of such an artery may be patent due to the development of a collateral circulation

By far the most important of these signs is narrowing of the arterial

lumen Normally the apparent width of a retinal artery compared with its accompanying vein is as 5 5 or 4 5 When the artery is thickened this ratio is decreased and may be about 3 5 or less There is no better way of expressing the average calibre of the retinal arteries than by giving the approximate arterio venous ratio

In benign hypertension it is rare to find more than notching of veins and narrowing of the arterial lumina white arterial fringes and obliteration of the lumen usually mean nephritic or malignant hypertension

It should perhaps be added that the appearance of the fundal vessels gives little indication of the state of the cerebral vessels the risk of stroke cannot be assessed from retinoscopy

Retinal hæmorrhage may be superficial, when it is linear or fan shaped in appearance or deep when it resembles a rounded smudge Both kinds may be seen in hypertensive retinopathy but the former is more common Hæmorrhages are unusual in essential hypertension and when present are usually minute They are not uncommon in nephritic hypertension and almost invariable sooner or later in the malignant type Just what causes these small hæmorrhages is not clear for the capillary blood pressure is normal in hypertension (Ellis and Weiss 1929–30) and in any case healthy capillaries can withstand astonishingly high pressures Hæmorrhage secondary to a venous thrombosis at an arterio-venous crossing is more easily understood

Thrombosis of a retinal artery or vein usually causes a defect in the visual field of the affected eye and thrombosis of the central artery or vein causes blindness Unfortunately retinal thrombosis is apt to be recurrent

Retinal exudates are of four distinct types (1) large hæmorrhages sometimes reveal eccentric soft white cores which may persist after absorption of the blood (2) soft fleecy patches scattered indiscriminately over the retina are characteristic of malignant hypertension (3) complete or incomplete star patterns composed of hard whitish particles or dots radiating from the macula may be seen in chronic nephritic or in malignant hypertension (4) in diabetes mellitus, the exudate is waxy sharply cut and scattered, resembling pale yellow confetti Small areas of retinal degeneration in old people should not be confused with exudates

When *papillœdema* is added to the signs of hypertensive retinopathy already described malignant hypertension should be diagnosed Conversely malignant hypertension should not be diagnosed in the absence of papillœdema (Ellis 1938) Although chronic nephritis may be responsible little is lost by making the other diagnosis for if there is papillœdema the course of the disease will certainly be malignant if acute nephritis and toxæmia of pregnancy can be excluded The appearances may be distinguished from those of cerebral tumour by the arterial changes by a macular star figure or by exudates independent of hæmorrhages

Papillœdema is usually associated with a high cerebro spinal fluid pressure but not invariably moreover higher C S F pressures are found

without papilloedema in cases of superior vena cava obstruction Evidence from experimental hypertension in rats suggests that papilloedema is due to cerebral oedema caused by intense vascular spasm and secondary increased capillary permeability (Byrom 1954) Occasionally, progressive blindness occurs

Examination of the heart usually reveals some degree of left ventricular hypertrophy The apex beat becomes displaced slightly to the left and downwards the cardiac impulse becomes heaving in quality and unusually easy to feel It is quite different from the short sharp thrust of the overacting heart for it is a quiet unhurried action giving the impression of great strength The hyperdynamic quality of the former may be compared with the first few strokes of a racing crew galvanised into urgent action by the sound of the starting signal the heaving impulse of left ventricular hypertrophy to the powerful steady drive maintained by the crew when it has settled down to a long hard struggle If, with due care, the apex beat cannot be located, left ventricular hypertrophy is unlikely even in obese subjects, unless masked by emphysema

Presystolic gallop rhythm is common with severe hypertension and means that the left ventricle is receiving atrial help to increase its diastolic stretch so that it may contract more powerfully The second sound at the base is accentuated and high pitched Functional aortic incompetence is not uncommon and may be associated with diastolic pressures of 130 to 170 mm Hg in other words it may not affect the circulatory dynamics It is due to dilatation of the aortic ring and may be compared with functional pulmonary incompetence in cases of pulmonary hypertension Pulsus alternans may sometimes be heard especially if there is a mitral systolic murmur (Levine 1948)

Auricular fibrillation is found in about 7 5 per cent of unselected hypertensive patients (Rothstadt 1938) and may precipitate congestive heart failure At first and particularly if untreated it may be paroxysmal but as a rule it soon becomes persistent especially in elderly subjects Permanent auricular fibrillation under digitalis control is less troublesome than paroxysmal fibrillation and tends to protect the individual from paroxysmal cardiac dyspnœa and acute pulmonary œdema Other rhythm changes are relatively rare but include auricular flutter paroxysmal tachycardia and all degrees of heart block

Limitation of cardiac reserve is indicated by undue breathlessness on exertion and by poor responses to effort tolerance tests Left ventricular failure develops sooner or later in the majority of those who survive the other hazards of hypertension and may be recognised by a history of orthopnœa paroxysmal cardiac dyspnœa or pulmonary œdema and by finding a diminished vital capacity maximum breathing capacity and lung volume exaggeration of respiratory intrathoracic pressure swings prolongation of the crude pulmonary circulation time an increased pulmonary blood volume and radiological evidence of chronic interstitial

(pulmonary venous congestion) as described on pages 273 to 279.

Congestive heart failure with elevation of the venous pressure hepatic distension and dependent œdema, follows left ventricular failure in practically all cases that survive other risks Not infrequently, patients with hypertensive heart disease develop congestive heart failure without previous orthopnœa and paroxysmal cardiac dyspnœa There are two chief explanations for this behaviour (1) Left ventricular failure may result in a diminished cardiac output which reduces the renal blood flow and leads to retention of sodium and water the increased blood volume then raises the venous pressure so that the clinical features resemble those of failure of both ventricles although the right ventricle itself may not be overloaded (2) As in mitral stenosis passive pulmonary hypertension resulting from an elevated left atrial pressure may lead to active pulmonary vasoconstriction when the pulmonary vascular resistance exceeds 10 units right ventricular failure may be expected It should be explained perhaps that the pulmonary artery pressure is not ordinarily raised in systemic hypertension of any type or severity provided there is no left ventricular failure (Lenegre and Maurice 1947)

The suggestion that the right ventricle is partly obstructed by displacement of the interventricular septum (Bernheim 1910) lacks proof but the grounds on which the existence of Bernheim's syndrome is now being rejected are premature and equally unconvincing It may clarify matters to restate the present position. The syndrome implies a severe left sided cardiopathy (such as hypertensive heart disease aortic valve disease mitral incompetence or cardiac infarction) with a form of left ventricular failure that presents clinically with a high venous pressure enlargement of the liver œdema and relatively little breathlessness but without orthopnœa, paroxysmal cardiac dyspnœa pulmonary œdema or radiological evidence of pulmonary venous congestion Bernheim's suggestion that a filling defect of the right ventricle caused by undue bulging of the interventricular septum might be responsible for the so called right ventricular failure was welcomed as a reasonable hypothesis to explain the physiological situation and after holding sway for forty years should not be abandoned without adequate proof to the contrary

Just as Eisenmenger's complex has had to be brought up to date by adding its most essential feature (a pulmonary vascular resistance at or above systemic level) so Bernheim's syndrome must be brought up to date by adding *absence of a high pulmonary vascular resistance a small right ventricle* and *considerable dilatation of the right atrium* As explained above the development of a high pulmonary vascular resistance (10 to 0 units) in cases of left ventricular failure can certainly prevent pulmonary congestive manifestations just as it can in mitral stenosis but in such instances the right ventricle is enlarged and the electrocardiogram may provide evidence of this in life This situation must be excluded before a diagnosis of Bernheim's syndrome is tenable The high resistance can be proved by

means of cardiac catheterisation in non ischæmic cases but the procedure is dangerous in patients with angina pectoris or previous cardiac infarction But if the pulmonary vascular resistance is not unduly high as in the case described by Selzer *et al* (1955) in which it was only 5 7 units what is protecting the lungs? Right ventricular failure should not occur from passive pulmonary hypertension (Wood 1954)

In some individuals with high left atrial pressures pulmonary congestive symptoms are curiously lacking despite the radiological demonstration of chronic interstitial œdema of the lungs but we are not concerned with these in the present discussion because one of the criteria upon which the modern diagnosis of Bernheim s syndrome rests is absence of this radiological sign

Selzer *et al* in their argument against the validity of the Bernheim concept compare the expected physiological situation with that in right sided constrictive pericarditis This is unsound partly because there is virtually no such thing as right sided constrictive pericarditis and partly because Bernheim s syndrome could not exist without left ventricular failure and a rise of left ventricular diastolic pressure A filling defect of the right ventricle implies impairment of a *diastolic* physiological function and the septum would not bulge unduly into the cavity of the right ventricle during diastole if the diastolic pressure relationship between the two ventricles was reversed Pick s disease however considered conventionally serves very well to illustrate the Bernheim concept In this disease the left atrial pressure is usually of the order of 20 mm Hg which in uncomplicated mitral stenosis would certainly be sufficient to cause pulmonary congestive symptoms Why then are these symptoms usually absent? The answer of course is because the cardiac output cannot rise sufficiently to raise the left atrial pressure well above the osmotic pressure of the plasma This is just what might be expected if left ventricular failure were complicated by a filling defect of the right ventricle

One way of proving whether the right ventricle is overloaded or suffering from a filling defect would be to raise or lower the right atrial pressure by tipping or other means if the right ventricle is overloaded raising its filling pressure should reduce its output and therefore lower the pulmonary systolic pressure and the mean left atrial pressure if the right ventricle is suffering from a filling defect then raising the right atrial pressure should increase its output and therefore raise the pulmonary systolic pressure and mean left atrial pressure Or one might study the effect of inspiration and expiration upon the pulmonary component of the second heart sound with an overloaded right ventricle P_2 should not be delayed by inspiration whereas with a filling defect of the right ventricle it should be so delayed

The cardiac output is low in hypertensive congestive heart failure but may be near normal at rest in isolated left ventricular failure moreover paroxysmal cardiac dyspnœa may occur as the output rises (page 274)

The size of the heart in hypertension bears a close relationship to the

duration of heart failure it is largest in essential hypertension when failure has been protracted least enlarged in chronic nephritic hypertension when death is due to renal failure or in those who die from apoplexy or from other non cardiac causes (Harrison and Wood 1949) Again serial skiagrams may show little alteration in the manifest size of the heart for long period in essential hypertension yet gross enlargement may develop rapidly when failure occurs This is not only a matter of cardiac dilatation because heart weights show similar correlation Slight to moderate left ventricular hypertrophy probably results from hypertension alone according to its degree and duration but gross enlargement which usually involves the right ventricle as well as the left is always due to protracted failure

Moderate hypertrophy should be regarded as a compensatory change of structure which is beneficial it helps the heart to perform more work (Dieckhoff 1936)

Electrocardiography provides the most accurate means by which the degree of left ventricular enlargement and stress may be assessed Leads facing the surface of the left ventricle, such as V and V_6 show high voltage and slightly widened R waves with depressed R T segments and inverted T waves (fig 16 01) This fundamental pattern is reflected in right

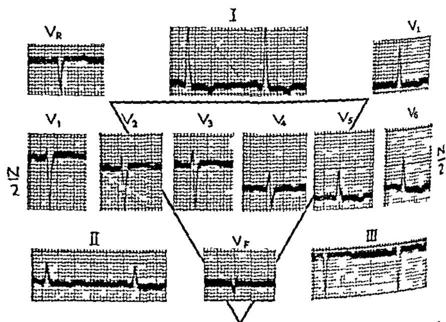


Fig 16 01—Electrocardiogram in a case of hypertensive heart disease (see text) The heart is electrically horizontal

ventricular surface leads such as V as small R waves followed by deep S waves the S T segment being elevated and the T wave invariably upright The heart is usually electrically horizontal left ventricular surface potentials being transmitted to the left arm right ventricular surface poten

tials to the left leg Lead V_L then resembles V_5 and V_6 lead V_F resembles V_1 Standard limb leads therefore show left axis deviation, lead I looking like V_L and lead III like V_F

When the heart is rotated clockwise on its longitudinal axis (viewed from below) the anterior part of the inter ventricular septum is displaced to the left and the transition zone shifts to the left of V_4 (fig 16 02) when the heart is rotated anti clockwise the transition zone moves to the right and QR complexes or dominant R waves with inverted T waves may be found as far across as V_3

When the heart is electrically vertical left ventricular surface potentials are transmitted to the left leg right ventricular surface potentials to the left

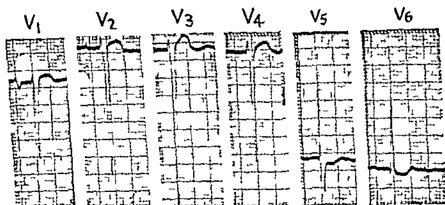


Fig 16 02—Electrocardiogram in a case of hypertensive heart disease with clockwise rotation about the longitudinal axis the transition zone is shifted to the left

arm Lead V_F then shows the tall R wave and inverted T whilst lead V_L has a prominent S wave Standard leads may then show right axis deviation with inversion of the T wave in leads 2 and 3

Concordant left ventricular preponderance in standard leads (fig 16 03) is due to a semi vertical electrical position of the heart Left ventricular surface potentials are transmitted to the left leg and standard leads show high voltage R waves and inversion of the T wave in all leads

The higher and wider the R wave in lead V_5–V_6 and the deeper the S wave in lead V_1 the bigger the left ventricle The pattern may be distinguished from left bundle branch block by the presence of Q in lead V_6 The cause of the R T segment depression and the T wave inversion is less well understood these changes may be associated with acute left ventricular stress without hypertrophy of the muscle although they usually result from both coronary disease is not responsible They are not altered by exercise or by transient reduction of the blood pressure to normal levels by means of hexamethonium or tetraethylammonium (Hayward 1948)

duration of heart failure it is largest in essential hypertension when failure has been protracted least enlarged in chronic nephritic hypertension when death is due to renal failure or in those who die from apoplexy or from other non cardiac causes (Harrison and Wood 1949) Again serial skiagrams may show little alteration in the manifest size of the heart for long periods in essential hypertension yet gross enlargement may develop rapidly when failure occurs This is not only a matter of cardiac dilatation because heart weights show similar correlation Slight to moderate left ventricular hypertrophy probably results from hypertension alone according to its degree and duration but gross enlargement which usually involves the right ventricle as well as the left is always due to protracted failure

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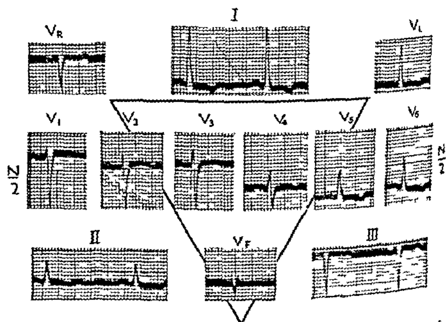


Fig 16 01—Electrocardiogram in a case of hypertensive heart failure (see text) The heart is electrically horizontal

ventricular surface leads such as V_2 as small *R* waves followed by deep S waves the S T segment being elevated and the T wave invariably upright The heart is usually *electrically horizontal* left ventricular surface potentials being transmitted to the left arm right ventricular surface p



(a) Anterior view the apex of the left ventricle is buried in the diaphragm



(b) Angiocardiogram in the second oblique position

Fig 16 04—Hypertensive heart disease showing left ventricular enlargement



(a) Anterior view



(b) Left anterior oblique position with barium in the œsophagus

Fig 16 05—Skiagram of a case of hypertensive heart disease showing unfolding of the aorta





(a) (b)

I ig 16 06 Compars n of th ronars stem in a n rm al (a) and a hyp rten ive heart (b) Th oron irs l ha e be n inje ted with a radio opaque gel (ee text)



(a)



(b)

Fig 16 07—Coronary systems of two cases of hypertensi e heart di ea e ith angina pect

(a) Sho ing occlusi e coronary atherosc cn (mixed ca e)

(b) Showing failure of the coronary vessels to enlarge with the heart

Angina pectoris occurs in 5 to 10 per cent of cases and may be due to associated coronary atherosclerosis or to relative coronary insufficiency. Conversely essential hypertension (past or present) has been found in 27 per cent of men and 71 per cent of women who present with coronary occlusion (Master 1953). Angina may be typical or it may tend to last longer than usual even up to an hour or so depending particularly upon transient rises of blood pressure such as occur, for example in paroxysmal hypertension strong emotion e g fear or anger and exposure to cold may provoke such an attack

It will be remembered that the coronary blood flow depends upon the mean blood pressure and upon the state of the coronary arteries During systole the large extra mural coronary vessels dilate forming a tense elastic reservoir the outflow being sealed by the intramural pressure The higher the systolic pressure the greater this elastic reservoir As the ventricles relax blood flows through the intra mural branches influenced not only by the aortic diastolic pressure but also by the elastic recoil of the superficial coronary arteries

Autopsy studies indicate that the coronary blood flow in essential hypertension is considerably increased In figs 16 06 the coronary systems of a normal and of a hypertensive heart are compared The vessels have been injected with a radio opaque substance at the calculated mean pressure and skiagrams have been taken at a fixed distance so that comparative measurements are valid The large and luxuriant coronary tree of the hypertensive case is typical of the series studied (Harrison and Wood 1949) It is probable that the coronary flow behaves like the blood flow through skeletal muscle and is usually increased in all forms of hypertension In cases of angina however skiagrams of the injected coronary vessels show either occlusive atherosclerosis (fig 16 07a) or a meagre coronary system which has failed to enlarge with the heart (fig 16 07b)

Renal behaviour varies greatly according to the type of hypertension In the essential variety renal failure is rare and when it does occur it is late usually in patients over 70 years of age Minor degrees of renal involvement however are common Traces of albumin, and hyaline casts are often found in the urine due to glomerular fault and diminished filtration may be revealed by inulin creatinine or urea clearance tests Tubular re absorption may be impaired resulting in polyuria and in diminished power of urinary concentration Nocturia may also be a feature

In malignant hypertension there is always a fast race between renal failure, cardiac failure and cerebral catastrophe The end is sometimes a combination of all three Nevertheless despite the early occurrence of renal failure it is rare for pronounced changes in renal function or for conspicuous urinary findings to precede the characteristic retinopathy (Wagener and Keith 1924) The converse is true of nephritic hypertension Nephrosclerosis in malignant hypertension differs from that found in

essential hypertension only in the presence of afferent glomerular arteriolar necrosis

In chronic nephritis there is usually considerable evidence of renal damage at a time when the heart is but little enlarged, and when the fundi are relatively normal Albumin, hyaline and granular casts and occasionally red cells, are found in the urine, inulin, creatinine and urea clearance are greatly diminished the blood urea may be raised and there is commonly polyuria nocturia, and failure of urinary concentration

Cerebral manifestations occur sooner or later in about one quarter of hypertensive cases *Cerebral hæmorrhage* is an ever present danger and may at any time cut short the life of the patient *Subarachnoid hæmorrhage* is by no means rare congenital deficiencies in the media or elastica of certain arteries, particularly those forming the circle of Willis with or without berry aneurysm giving way to the high pressure *Cerebral thrombosis* may also occur but depends more upon associated cerebral atherosclerosis

Hypertensive encephalopathy is characterised by attacks of severe head ache vomiting coma or convulsions lasting for hours, with or without transient localising signs and is an important complication of malignant hypertension It is probably due to local or general cerebral ischæmia and œdema secondary to intense cerebral vascular spasm and increased capillary permeability (Scheinker 1948 Byrom, 1954) It should be understood that the normal cerebral blood flow in uncomplicated malignant hypertension implies intense cerebral vasoconstriction for if the cerebral vascular resistance remained normal the cerebral blood flow would be torrential with blood pressures in the region of 260/150 The rapid recovery that follows appropriate treatment (*vide infra*) and the ease with which appropriate prophylactic treatment prevents attacks deny both cerebral hæmorrhage and cerebral thrombosis although both may have to be excluded in the first instance

Deterioration of higher cerebral function has already been mentioned when severe it is usually due to associated atherosclerosis and ischæmia Occasionally however multiple pin point hæmorrhages scattered widely throughout the frontal lobes are found at autopsy and provide adequate explanation for dementia

Hæmorrhages elsewhere are not uncommon and include epistaxis hæmoptysis and hæmatemesis Whilst some local predisposing factor would seem probable, nothing significant is usually found Clinical diagnosis in such cases may be obscure at first, for hypertension may not be recognised owing to the fall of blood pressure which accompanies the hæmorrhage Moreover, when hæmodilution is slow, so that the hæmoglobin or hæmatocrit level is but little reduced the apparently normal blood pressure may lead to gross error of judgment concerning the size of the hæmorrhage Routine examination of the ocular fundi tends to prevent such mistakes

DIFFERENTIAL DIAGNOSIS

If the blood pressure is found to be raised relative to standards already discussed a diagnosis of hypertension can be made and differential diagno is is concerned only with its cause

Acute nephritis should be obvious enough The distinction between *toxæmia of pregnancy* and essential hypertension in a pregnant woman is not always easy unless the previous or subsequent history is known Essential hypertension tends to be relieved during the second trimester for the peripheral resistance is lowered during a normal pregnancy Albuminuria sodium and water retention œdema elevation of the venous pressure breathlessness and a demonstrably rising blood pressure all indicate toxæmia of pregnancy It should be borne in mind however that the incidence of toxæmia in women with chronic essential hypertension is about seven times that in previously normal women (Browne 1947) so both may well be present *Coarctation of the aorta* is easily recognised if the femoral arteries are palpated as a routine *Cushing s syndrome* is suggested by obesity purple striæ high coloured moon facies hirsutism and amenorrhœa further studies are needed to elucidate the cause of the pituitary basophilism Functional overactivity of the adrenal cortex may lead to a rather similar syndrome (Shrœder *et al* 1949) A *hyperkinetic circulatory state* with high systolic pressure and less conspicuously raised diastolic pressure should be recognised by the tachycardia throbbing digital vessels bounding pulse and overacting heart Its cause may not be at all obvious and it should certainly not be attributed to an anxiety state or functional hyperadrenalism by a process of exclusion but only on positive grounds Hyperthyroidism arteriovenous fistula and Paget s disease of bone may be responsible for a hyperkinetic rise of blood pressure especially when there is coincidental atherosclerosis which increases the more proximal vascular resistance The degree of vasodilatation in hepatic failure and beri beri the reduced blood volume in severe chronic anæmia and the relatively slight increase of cardiac output in hypoxic cor pul monale do not encourage hyperkinetic systemic hypertension *Phæo chromocytoma* with a predominant outpouring of adrenaline rather than noradrenaline can cause a hyperkinetic circulatory state with chiefly systolic hypertension a test dose of rogitine is therefore advised in these difficult cases *Functional hyperadrenalism* should respond to rogitine equally well Personal experience suggests that there is also a non psychiatric form of hyperkinetic hypertension of as yet undetermined cause

Paroxysmal hypertension due to phæochromocytoma may be suggested by the history and confirmed by the rogitine or histamine type of test and by finding an excess of catechol amines in the plasm or urine (page 770)

The differential etiological diagnosis of persistent hypertension due to a high peripheral vascular resistance (after excluding phæochromocytoma and Cushing s syndrome) lies between chronic pyelonephritis other surgical kidneys chronic nephritis and essential hypertension

Chronic pyelonephritis may be suggested by the history, the absence of hypertension in the parents, pus cells and micro organisms in the urine early limitation of tubular concentrating power and the development of the malignant course in a relatively young subject (Brod 1955) Whether routine pyelography is justified when there is nothing to suggest chronic unilateral pyelonephritis is at least debatable Out of 2 035 routine pyelograms in subjects with persistent hypertension reported by Ratcliff *et al* (1947) less than 0 8 per cent were found to have an unsuspected unilateral renal lesion of a kind that led to nephrectomy and of this small number only about a third were so relieved of hypertension Since pyelography is not entirely without risk it is difficult to believe that its routine use is either wise or economically defensible for the sake of one patient out of 300 investigated Perhaps it should be restricted to those cases that might reasonably be suspected of having chronic pyelonephritis on the grounds given above

Chronic nephritis (chronic pyelonephritis and other surgical kidneys having been excluded) is a more likely etiological diagnosis than essential hypertension if impairment of renal function is far in advance of cardiac or cerebral disturbance or if renal failure occurs without heart failure in subjects under 60 years of age The differential etiological diagnosis between chronic nephritis and essential hypertension is no longer academic when hypertension is in the malignant phase

Malignant hypertension itself is diagnosed whenever there is papilloedema Etiologically almost any form of hypertension may take this course including acute nephritis visceral angiitis toxæmia of pregnancy phæochromocytoma Cushing s syndrome pyelonephritis chronic nephritis and essential hypertension only coarctation of the aorta is exempt

COURSE AND PROGNOSIS

The hypertension of *acute nephritis* is nearly always transient in those that recover After a latent interval which varies from a few weeks to very many years the blood pressure rises again in those that develop chronic nephritis The prognosis is then grave the mortality rate in men being six times that which would be expected in unaffected men of the same age group (Frant and Groen 1950)

Follow up studies on cases with *toxæmia of pregnancy* reveal that 50 per cent develop permanent essential hypertension (Light 1948) It is not clear however whether pre eclampsia is responsible for the subsequent hypertension or whether pregnancy merely precipitates the onset of essential hypertension The prognosis once persistent hypertension has developed appears to be the same as for essential hypertension

Perhaps the best follow up studies of persistent hypertension in the literature are those by Janeway (1913) Blackford Bowers and Baker (1930) and Bechgaard (1946) Janeway found that one half of 458 patients were

dead within five years and three quarters within ten years of the onset of symptoms Blackford Bowers and Baker reported a 56 per cent mortality (70 per cent of the men 9 per cent of the women) amongst 222 cases within five to eleven year Of Bechgaard s 1 000 patients 41 per cent of the men and 22 4 per cent of the women were dead within five to ten years The better outlook in women was emphasised in all three articles Bechgaard found the mortality rate of hypertensive men was 2 9 times and women 1 4 times that of the general population and was similar in all age groups (excluding renal cases)

Apart from sex the chief factors affecting prognosis include the type of hyperten ion the degree of retinopathy the height of the diastolic blood pressure and the state of the heart The natural outlook in malignant hypertension is uniformly bad few cases surviving more than one or two years and the average only 8 4 months after the diagnosis is fir t made (Schottstaedt and Sokolow 1953) Chronic nephritic hypertension also has a grave prognosis the mortality rate being about three times that of essential hypertension (Frant and Groen 1950) This is partly because renal hypertension is often a late manifestation of chronic kidney disease—hence the frequency of a normal sized heart in this group

Wagener and Keith (1939) correlated life expectancy with changes in the ocular fundi they followed the course of 200 patients for five to nine years The survival rate according to whether retinal changes were mild moderate severe or gross was 80 per cent 35 per cent 9 per cent and nil respectively When retinopathy was gross and included papillœdema, 80 per cent died within one year

Although the height of the systolic blood pressure is often said to matter little Sarre and Lindner (1948) found that in a series of 166 cases observed over a period of seven years 48 per cent of those with systolic pressures under 200 mm Hg survived compared with only 11 per cent of those with systolic pressures over 200 mm Hg It is generally agreed that high diastolic pressures are sinister in the series just quoted for example only 6 per cent of those with diastolic pressures above 140 mm Hg when first seen survived seven years

Cardiac behaviour in hypertension is determined by the amount of extra work involved and by the ability of the heart to cope with it it is chiefly influenced by the rapidity of hypertensive development by the size and strength of the left ventricle and by the efficiency of the coronary blood flow The best defence is put up by a placid patient of voluntary or enforced sedentary habits and occupation who has a naturally strong left ventricle with a good coronary blood flow when hypertension is neither too severe nor too sudden Under such circumstances the heart enlarges but little over the years failure is indefinitely deferred, and the patient remains free from cardiac symptoms The worst defence leading to rapid failure and perhaps to early death occurs in an excitable individual of active physical habits and strenuous occupation who tries to cope with a rapidly develop-

ing and extreme hypertension with an unprepared left ventricle indifferently nourished by a mean coronary system

Evidence of any cardiac abnormality e g diminished cardiac reserve angina pectoris enlargement or electrocardiographic changes at once doubles or trebles the mortality rate (Bechgaard 1946) Inversion of the T wave in left ventricular surface leads or their equivalent is particularly grave at least 60 per cent of such cases being dead in an average of eight months from the time of its discovery (Rykert and Hepburn 1935) Auricular fibrillation means death within two years in 80 per cent of cases (Rothstadt 1938)

Hypertensive heart failure is characteristically left ventricular at first and limits natural life expectancy to about eighteen months Systemic congestion follows sooner or later Several congestive attacks usually occur each responding less satisfactorily to treatment than its predecessor The patient finally sinks into a stuporose condition with chronic venous congestion hepatic engorgement and dependent dropsy the blood pressure falls Cheyne Stokes breathing develops and death comes slowly Heart disease is responsible for death in 33 per cent (Janeway 1913) to 55 per cent (Bell and Clawson 1928) of hypertensive cases stroke in 7 2 per cent (Paullin *et al* 1927) to 16 per cent (Bechgaard 1946) uræmia in 10 per cent (Bechgaard 1946)

The average life expectancy in uncomplicated benign hypertension of slight or moderate grade is about fifteen years (Fahr 1928) Obese subjects do as well or better than those with normal weight probably because their blood pressures are not as high as they seem when measured by means of standard cuffs Spontaneous recovery occurred in 5 4 per cent of Bechgaard s series (2 per cent of the women 13 per cent of the men) but in none of those seen by Blackford Bowers and Baker After five to ten years 58 per cent of Bechgaard s cases were free from symptoms or only slightly inconvenienced

Only about 0 2 per cent of cases of essential hypertension later become malignant but 8 per cent of cases of chronic pyelonephritic hypertension do so

TREATMENT

It must be said at once that as yet there is no satisfactory treatment for essential or malignant hypertension When nephritic hypertension is due to a unilateral lesion such as chronic pyelonephritis nephrectomy has proved curative in 19 per cent of 242 cases (Smith 1948) but otherwise it can be but little influenced Moreover a causal relationship between a unilateral renal lesion and hypertension cannot be taken for granted and before advising nephrectomy it is as well to make sure that neither parent was hypertensive (Platt 1947) Normal renal function is also a necessary condition for successful nephrectomy for severe hypertension may have so damaged the vessels of the originally healthy kidney as to have made it

ischæmic and so to have established a vicious circle (Wilson and Byrom 1941) Good results from nephrectomy may be expected in 5 to 50 per cent of cases when the renal lesion is chronic uncomplicated unilateral pyelonephritis (Ratcliff *et al* 1947 Pickering and Heptinstall 1953)

The hypertension of Cushing s syndrome and that of phæochromo cytoma both respond to removal of the offending tumour and that due to coarctation of the aorta to surgical repair

For essential hypertension there are six main lines of treatment (1) conservative (2) the low sodium or rice diet (3) a miscellaneous group of drugs acting on the central nervous system including rauwolfia veratrum hydrazinophthalazine and thiocyanate (4) adrenergic blocking agents such as hydergine (5) lumbo dorsal sympathectomy (6) ganglionic blocking agents such as hexamethonium and pentolinium

Conservative When the grade of hypertension is mild or moderate and when the prognosis is judged to be good on criteria previously outlined radical medical or surgical treatment is hardly justified but this does not mean that nothing else need be done Conservative treatment seeks to cor rect adverse factors and to prevent complications or deterioration

If circumstances permit it is a good plan to begin treatment by putting the patient to bed, and to keep him there until the blood pressure has reached a static level Symptoms usually disappear quickly and the patient gains confidence During this time renal function may be fully and con veniently investigated also the reaction of the blood pressure to bed rest gives useful diagnostic and prognostic information innocent labile types falling quickly to normal nephritic and malignant hypertension responding least

Patients should then be advised to live at a lower tempo they should learn to refuse extra commitments and to relinquish the least important or most irksome of those they already have they should keep Saturday and Sunday free for relaxation should have at least nine hours rest in bed every night and should insist on proper holidays each year preferably six weeks Long working hours heavy mental or physical stress and the general rush hurry and struggle of modern life must be avoided or reduced Occupation may require modification but it is rarely practicable to change it radically Sudden effort especially in the cold or after a heavy meal should be avoided straining at stool should be prevented by regular habits and if necessary by the use of liquid paraffin Alcohol in moderation is permitted, smoking should be strictly limited

Mental relaxation may be impossible without sedatives or psychiatric help Phenobarbitone ½ to 1 grain (32 to 64 mg) t d s may be prescribed at times of unavoidable anxiety alternated with potassium bromide 5 to 10 grains (0 32 to 0 65 G) t d s Psychiatric help is invaluable not necessarily from a psychiatrist but by any experienced physician with the requisite knowledge Many of the symptoms ascribed to hypertension are more often due to anxiety moreover hypertensive subjects usually have hyper-

reactions to anxiety in the sense that their blood pressures rise unduly (Hines 1940)

Symptoms attributed to hypertension at the menopause may respond to oral stilbœstrol 0 5 mg ethinylœstradiol 0 02 mg dienœstrol 1 mg or mepilin tab 1 daily although the blood pressure does not fall an associated anxiety state is also common at this time

Obese patients tend to do well on a weight reducing diet One day's bed rest with semi starvation per week diet then being limited to fresh fruit fruit juice and water only may be most helpful or such a regime may be instituted at less frequent intervals when the patient feels the need of it

With this simple regime 60 per cent of patients with essential hypertension remain free from symptoms until cerebral cardiac or renal complications arise.

Venesection has been advocated in the past and is still practised from time to time It is only justified in phlethoric cases associated with polycythæmia In essential hypertension its effect is fleeting the blood pressure often regaining its previous level within twenty four hours In malignant hypertension and in chronic nephritis venesection is contra indicated for some degree of anæmia is usually present in both conditions

Encephalopathy may be treated conservatively by means of rest and vigorous dehydration Vestibular disturbances are relieved by dramamine or avomine 25 mg three times daily (Goldman *et al* 1951) Heart failure responds to rest digitalis mercurial diuretics aminophylline and a low sodium diet Renal failure resists all therapy

Low sodium diet Although Allen and Sherrill in 1922 showed that a low salt diet was a potent means of lowering the blood pressure efficient dietetic treatment was not generally practised until re introduced by Kempner in 1944 Kempner's fruit rice diet consists essentially of fruit in any form fruit juices rice sugar and a little milk, it contains approximately 2 000 calories 20 G of protein 5 G of fat 200 mg of chloride and 150 mg of sodium (Kempner 1946) Lean meat fish and non leguminous vegetables without salt and fat may be added when the blood pressure has been satisfactorily controlled (Kempner 1948) Of 777 cases so treated the majority severe 70 per cent were unquestionably improved in an average time of three to four months (Kempner 1949) objective evidence included a fall in the sum of the systolic and diastolic blood pressure of at least 40 mm Hg disappearance of papillœdema and of retinal hæmorrhages and exudates restoration of an upright T wave in standard lead I (achieved in 50 per cent of cases in which it was previously inverted) and an appreciable reduction in the transverse diameter of the heart (51 per cent of 286 cases radiographed showed a reduction of about 6 per cent 37 per cent a reduction averaging 14 per cent and 6 6 per cent a reduction averaging 24 per cent)

The efficacy of a diet very low in sodium was confirmed in rats with experimental hypertension by Grollman and Harrison (1945) and in

human essential hypertension by Grollman (1945) It is now generally believed that its effect depends chiefly on its low sodium content (Pickering 1952)

Treatment of this kind is invaluable to relieve hypertensive crises including encephalopathy and severe retinopathy with impairment of vision it is also the best means of rapidly controlling left ventricular failure and congestive heart failure but its monotony precludes its routine use in uncomplicated essential hypertension for life expectancy may be ten years or more nor can it be used when there is gross impairment of renal function, for it may then precipitate uræmia For long term treatment however, a modified low sodium diet containing between 0 5 and 1 G. of sodium per day is advised With the help of lemon and herbs of all kinds such a diet (page 303) is well tolerated by the majority of patients whose personal experience has demonstrated its value and after six to twelve months some of them develop an active dislike towards salt A modified diet of this kind is insufficient by itself to control severe hypertension but it is a helpful adjunct to other forms of treatment and is imperative in cases with heart failure

Rauwolfia serpentina

Although a preparation of the root of rauwolfia serpentina has been used in India as a sedative since ancient times its value as a hypotensive agent has only recently been demonstrated (Vakil 1940 1949 1955 Bhatia 1942) The isolation of reserpine one of the most active of the rauwolfia alkaloids by Muller Schlittler and Bein (1952) was a notable advance

Reserpine 0 25 mg, is as active as 50 mg of the dried extract and more or less equivalent to 1 or 2 mg of preparations such as rauwiloid and hypertane which contain several of the other alkaloids of rauwolfia The initial dose of reserpine (serpasil) is 0 25 mg t d s, but it may be increased up to 0 5 mg t d s, or reduced to as low as 0 1 mg daily according to the response There can be no doubt that reserpine is a moderately potent hypotensive agent (Vakil 1953) It appears to act on the vasomotor centre itself in the hypothalamus A spate of literature has confirmed Vakil s results (e g Wilkins and Judson 1953)

Side effects include sinus bradycardia nasal congestion looseness of the bowels gain in weight coarse tremor or shakiness of the limbs vivid dreams drowsiness and mental depression

Bradycardia is beneficial in cases that present initially with hyperkinetic features and is never a disadvantage *Nasal congestion* may be very uncomfortable and should be treated with a suitable vasoconstrictor spray (such as privine) The *tendency to diarrhœa* helps to correct constipation in patients who are also treated with hexamethonium or pentolinium and is otherwise innocuous *Gain in weight* is due partly to the development of a hearty appetite and partly to retention of salt and water Both are serious

disadvantages the former particularly in cases with coincident coronary disease the latter when there is hypertensive heart failure (McGregor and Segal 1955) Dexamphetamine 5 mg one hour before breakfast and lunch may correct the increase of appetite and combat serpasil depression but *theoretically it would seem undesirable and is not advised until trials have* established its safety in these cases A low sodium diet given in conjunction with reserpine therapy prevents serious water retention *Shakiness of the limbs* is rare with doses not exceeding 0 25 mg t d s and usually disappears if the dose is reduced Coarse tremor seems to be Parkinsonian in type *Drowsiness* is beneficial at night but may interfere with efficiency by day the midday dose may then have to be withheld *Mental depression* may be intense and calls for immediate withdrawal of the drug for reducing the dose will not suffice This is fortunately unusual but must never be disregarded It has been suggested that depression is more common with reserpine than with preparations containing some of the other rauwolfia alkaloids but this has not yet been fully substantiated

Reserpine is not anti thyroid and does not increase the blood lipid *per se* As a rule coincident angina pectoris is not influenced by the treatment aggravation when it occurs may be attributed to gain in weight There is no evidence that the renal blood flow is reduced by rauwolfia alkaloids

Veratrum

Veratrum viride in the form of its powdered dry rhizome and roots was re introduced as a hypotensive agent for the clinical treatment of essential hypertension by Hite (1946) and Freis and Stanton (1948) A stable mixture of alkaloids biologically standardised was called veriloid (Stutzman *et al* 1949) and was found to be more easily managed clinically (Wilkins *et al* 1949) With initial doses of 2 mg t d s after meal increased gradually to 12 or 16 mg a day the blood pressure can be lowered in about two thirds of hypertensive cases (Kauntze and Trounce 1951) But side effects are the rule and include nausea and vomiting weakness and malaise and occasional collapse In the author s experience the patient s lack of well being while on veriloid precludes its long term use especially since it does not rank highly as a permanent hypotensive agent

Veratrum album has proved more valuable perhaps in that it has given us an active pure alkaloid protoveratrine (Krayer *et al* 1944 1946) which when given intravenously in doses of 0 1 to 0 15 mg may produce a profound fall of blood pressure in hypertensive patients (Meilman and Krayer 1950) thus it may be used intravenously with advantage in hypertensive crises For maintenance treatment protoveratrine is usually given by mouth in doses of *0 4 to 2 0 mg* three times daily after meal start with the smallest dose and gradually increasing it until the desired therapeutic effect is achieved or until the limit of tolerance is reached Toxic symptoms, similar to those of veriloid are all too common and the

number of cases that can be successfully treated is less than 25 per cent (Doyle and Smirk 1953 Currens Myers and White 1953)

Veratrum like rauwolfia appears to act directly on the central nervous system (Stutzman Simon and Maison 1951)

I Hydrazinophthalazine is another hypotensive agent which may act centrally It has been given by mouth in doses of 50 to 150 mg four to six hourly but an appreciable fall in blood pressure is obtained in relatively few cases and side effects may be formidable—chiefly severe headache tachycardia and anxiety or depression (Shroeder 1952) moreover good results are transient (Johnson *et al* 1952) A short experience of this drug was sufficient for the author to abandon it permanently

Thiocyanates Thiocyanate was originally introduced as a hypotensive agent by Treupel and Edinger (1900) but gained no immediate favour in view of the difficulty experienced in avoiding serious toxic symptoms Considerable interest was taken in the drug however when Barker (1936) showed that the dose could be properly controlled if the thiocyanate blood level was estimated weekly The normal serum thiocyanate ranges between 0 and 2 77 mg per cent and is not altered in hypertension (Connell Wharton and Robinson 1946) Levels above 15 mg per cent are dangerous and those between 12 and 15 mg per cent are risky Toxic symptoms include weakness anorexia indigestion nausea vomiting limb pains impotence purpura dermatitis goitre thrombophlebitis mental lethargy and confusion In fatal cases dysarthria verbal aphasia convulsions hallucinations delirium and mania have usually preceded death by three to nineteen days (Del Solar *et al* 1945) Progressive anæmia and emaciation have been attributed to chronic poisoning after five to ten years continuous therapy (Wald Lindberg and Barker 1939)

The potassium salt was given by mouth in initial doses of 2 to 3 grains (0 13 to 0 2 G) three times daily after meals The serum thiocyanate was measured on the seventh day and then at weekly intervals subsequent dosage being regulated as follows

Thiocyanate level	*Dosage recommended*
Under 5 mg per cent	2 to 3 grains (0 13 to 0 2 G) t d s
5 to 7	1 5 grains (0 1 G) t d s
7 to 10	1 grain (64 mg) t d s
Over 10	Stop drug for one week

The lowest blood level compatible with a satisfactory hypotensive effect was maintained for three to six months Further courses were given as desired

The drug was said to be unsafe in patients over 60 years old who had had cerebral or other thrombosis or who had poor renal function but Watkinson and Evans (1947) observed no ill effect in fifteen patients

over 60 nor in sixteen cases of malignant or chronic nephritic hyper tension

Thiocyanates were particularly recommended for labile hypertensives who complained of headache and giddiness (Hines 1946) but they were also used for severe or gross cases unsuitable for lumbo dorsal sympathec tomy and as an adjunct to surgical treatment Clinical benefit associated with a significant fall of blood pressure was claimed in about 60 per cent of cases (Watkinson and Evans 1947) This figure is not impressive when it is recollected that Bechgaard found that 58 per cent of 1,000 persistent hypertensives did well without treatment Carefully controlled observations such as those by Rusken and McKinley (1947) are more convincing and throw considerable doubt on the efficacy of thiocyanates It is well to remember that Pauli (1903), who is usually credited with introducing thiocyanate for the treatment of hypertension actually used the drug in the hope that it would prove superior to bromide in allaying anxiety symptoms and reported singular success in this respect Whether thiocyanate acts in this way or whether it has a more specific central hypotensive effect is still unknown but it is now considered too toxic for routine therapy and has been largely abandoned

Adrenergic blocking agents

Some confusion is attached to words like sympatholytic and adrenolytic, and it may help to define these terms A drug that blocks the response of effector cells to peripheral sympathetic nerve stimulation is said to be sympatholytic and since noradrenaline is the normal chemical mediator between the sympathetic nerve ending and the effector cell a sympatholytic substance is necessarily an adrenergic blocking agent A substance that blocks excitatory responses to *circulating* adrenaline and noradrenaline is said to be adrenolytic rather than sympatholytic but of course is also a adrenergic blocking agent The difference in actions between the two groups of drugs (although they always overlap to greater or less degree) is well exemplified in some of the diagnostic tests for phæochromocytoma For this purpose the best drugs are adrenolytic rather than sympatholytic and include benzodioxane and phentolamine (rogitine) dibenamine dibenzyline and ilidar have too powerful a sympatholytic effect to be reliable for this may lower the blood pressure in any kind of hypertension As therapeutic agents in essential hypertension it is the sympatholytic rather than the adrenolytic action that is needed and to this end hydergine is perhaps the best of the adrenergic blocking agents

Hydergine (1 ml) contains 0 1 mg of each of the three dihydrogenated alkaloids of ergotoxine (dihydroergocornine dihydroergocrystine and dihydroergokryptine) Dihydroergocornine or hydergine may be given in doses of 0 05 to 0 1 mg intramuscularly or 0 1 to 0 5 mg orally three times daily (Freis *et al* 1949 Gibbs 1952) but seems to lose its effect after a few weeks (Moister Stanton and Freis, 1949)

Dibenamine priscoline and rogitine are of little value (Nickerson 1951)

Lumbo dorsal sympathectomy In recent years numerous attempts have been made to lower the blood pressure by surgical means The only operation that has proved eminently successful is nephrectomy in those relatively rare cases in which hypertension is due to unilateral renal disease such as chronic pyelonephritis Of other surgical measures the best known is lumbo dorsal sympathectomy as elaborated by Smithwick (1940) This consists of bilateral resection of the whole sympathetic chain from D8 to L2, including preganglionic fibres ganglia and splanchnic nerves The object is to release as much vasoconstrictor tone as possible to prevent renal cortical vasoconstriction to produce postural hypotension and of course to lower the basal blood pressure if possible With these aims there has been an increasing tendency to extend Smithwick s operation and a number of surgeons e g Grimson (1947) and Boyd (1948) favour either total or subtotal paravertebral sympathectomy splanchnicectomy and cœliac ganglionectomy

The results of these various procedures have been fair The operative mortality has averaged 3 9 per cent but about 25 per cent have died during the period of post operative observation (usually three to five years) There is no doubt that headache dizziness and other symptoms may be alleviated the blood pressure lowered the electrocardiogram improved the heart size reduced and retinopathy diminished by such means (Peet *et al* 1940) objective improvement of one kind or another has been demonstrable in about 66 per cent of cases (Smithwick 1944 1949)

In a series of 400 cases operated on for hypertension at the Massachusetts General Hospital (F M sex ratio 1 8 1) follow up studies showed that after one year postural hypotension had virtually disappeared after two years 38 per cent were improved and after five years 8 of 100 cases had normal blood pressures 13 had significantly reduced blood pressures 52 were much the same and 27 were dead (Evelyn *et al* 1949)

Of 143 cases of malignant hypertension treated by splanchnic resection by Peat and Isberg (1948) 21 6 per cent were still alive and free from papillœdema five years later the operative mortality was 10 per cent and no patient with moderate or marked impairment of renal function or with considerable cardiac enlargement did well

Although the long term results of surgical treatment were indifferent their historical value should not be underestimated for sympathectomy first proved that the blood pressure in essential hypertension could be permanently lowered occasionally even to normal and that lowering the blood pressure abolished the malignant reaction improved the patient s health and prolonged life thereby disproving the ill founded theoretical objection that to lower the blood pressure in essential hypertension without dealing with the disease itself (whatever that was supposed to mean) was unphysiological

Surgical sympathectomy thus opened the way to medical sympathectomy

and encouraged pharmacological research into blood pressure lowering drugs of all kinds

Ganglionic blocking agents

The demonstration by Burn and Dale in 1915 that tetraethylammonium ions inhibited transmission of all sympathetic and parasympathetic nerve impulses at the autonomic ganglia and the realisation how this action might be exploited (Acheson and Moe 1945) opened the way to medical sympathectomy Normally all autonomic impulses are chemically transmitted by means of acetylcholine which is liberated by the preganglionic nerve terminal and which then excites the ganglionic cells Ganglion blocking drugs prevent acetylcholine from acting on the ganglion cells (Paton 1951) In doses of 3 to 5 mg per kilo intravenously or about 10 mg per kilo intramuscularly tetraethylammonium releases vasoconstrictor tone both the blood pressure and venous pressure fall especially in the upright position the peripheral blood flow increases the skin temperature rises and the heart rate quickens These effects may be reversed immediately by peripherally acting adrenergic drugs such as noradrenaline Simultaneous parasympathetic block results in temporary paralysis of the gut and bladder dry mouth dry skin, dilatation of the pupils and loss of accommodation (Berry *et al* 1946 Lyons *et al* 1947) Peripherally acting cholinergic drugs such as acetylcholine mecholyl etc reverse these effects

Pentamethonium iodide (C5) and *hexamethonium iodide* (C6) or bromide introduced by Paton and Zaimis (1949) were found to be more powerful and more prolonged ganglionic blocking agents than T E A and were soon tried clinically for the relief of hypertension (Arnold and Rosenheim 1949 Burt and Graham 1950 Turner 1950) None of these early reports was enthusiastic fears that merely lowering the blood pressure was unphysiological still lingered postural hypotension and fainting turns were regarded as serious drawbacks and the side effects from parasympathetic blockade were troublesome and occasionally dangerous In New Zealand however Smirk (1949) had perhaps a more enlightened view believing that the chief danger of hypertension was the high blood pressure itself however produced and that the object of treatment was to lower the blood pressure efficiently and keep it lowered postural hypotension properly harnessed became an asset rather than a liability and in conjunction with a low sodium diet methonium halides soon became the treatment of choice for the majority of cases of severe hypertension (Restall and Smirk 19 Smirk 1950 Smirk and Alstad 1951)

Hexamethonium bromide (vegolysen) may be given by subcutaneous injection in initial doses of 15 to 20 mg approximately three times daily the patient is preferably propped up in bed or may have the head of the bed raised on blocks so that orthostatic hypotension may be quickly recognised and corrected if too severe by lying the patient flat The blood

pressure should be recorded hourly both lying and standing Day by day the dose is increased by 10 to 20 mg according to the reaction and the rate at which tolerance develops the final dose may be 100 to 200 mg three times daily, but may have to be limited owing to side effects (*vide infra*) The objective is to maintain the blood pressure around the upper limit of normal when the patient stands up and to maintain it at this level for as long as possible during waking hours without causing serious side effects

Oral treatment requires doses of 250 to 750 mg thrice daily half to one hour before meals Unfortunately hexamethonium is very irregularly absorbed from the gut so that the correct dose is more difficult to arrive at and serious side effects may occur occasionally without warning

After a suitable single subcutaneous or intramuscular injection the clinical effect begins in 10 to 15 minutes and persists for several hours Within 24 hours 90 per cent of the drug is recoverable from the urine (Harrington 1953) Glomerular excretion is necessarily retarded in the presence of impaired renal function and if the blood urea is raised doses should be correspondingly small and infrequent if the drug is used at all

Undesirable side effects include constipation rarely intestinal paralysis retention of urine (particularly in patients with enlarged prostates) dry mouth, and disturbance of vision due to difficulty in accommodation The most dangerous of these is paralytic ileus which should be treated immediately with prostigmine 1 5 to 2 mg intravenously or intramuscularly and repeated two hourly if necessary no further doses of hexamethonium being given for at least 48 hours Laxatives are usually required as a routine to combat the tendency to constipation and patients should be advised to open their bowels before the morning dose of hexamethonium When serpasil is also used to help lower the blood pressure constipation is less troublesome Special reading glasses should be provided to compensate for the loss of accommodation

Weakness dizziness and pallor when standing still is due to orthostatic hypotension, and can be counteracted by walking about or lying down if dizziness is severe or if there is actual syncope the dose of hexamethonium should be reduced

Since bromine constitutes about 44 per cent by weight of *hexamethonium bromide* doses of 2 or more Grams per day orally are likely to result in symptoms of bromism sooner or later especially when patients are also on the low sodium diet These occur when the blood bromide exceeds 150 mg per cent and sometimes when it is only 75 to 100 mg per cent (Goodman and Gilman 1941) Hexamethonium iodide has a similar drawback in respect of iodism and the chloride is hygroscopic but the bitartrate 300 mg of which is equivalent to 250 mg of the bromide has none of these defects and is usually well tolerated Nevertheless with doses under 2 G daily hexamethonium bromide is preferred for its sedative action is an advantage

Pentolinium tartrate (M & B 2050 A or ansolysen) is about five times more potent and lasts one and a half times longer than hexamethonium (Wien and Mason 1953) moreover it is better absorbed from the gut more consistent results follow oral therapy (Maxwell and Campbell 1953) and hypertensive symptoms and complications (such as retinopathy) are controlled more swiftly than with hexamethonium (Smirk 1953)

If given by injection the initial dose should not exceed 4 mg, and increments should be small (2 mg) The initial oral dose is 20 to 40 mg three or four times daily half an hour before meals and this should not be increased by more than 20 mg per dose per day Management is otherwise the same as when using hexamethonium

Combined methods of treatment

The best all round results in the treatment of hypertension are undoubtedly obtained by combining rest the low sodium diet rauwolfia alkaloids and pentolinium by mouth (Smirk *et al* 1954) The treatment should be pressed home at the start until the blood pressure is normal or not above 160/90 in the standing position two hours after the last dose of pentolinium

The amount of each of the four therapeutic agents should then be adjusted to suit the patient until undesirable side effects are minimal and the regime tolerable and compatible with a reasonably active and enjoyable life This is usually possible while maintaining a good measure of control of the blood pressure

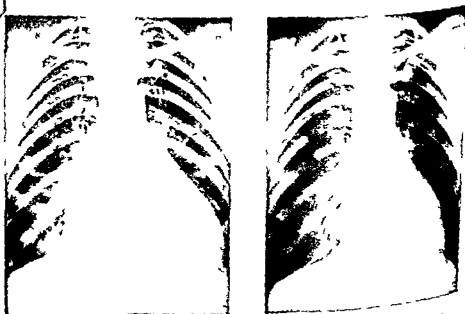


Fig 16 08—Skiagram (a) before and (b) after treatment of hypertensive heart failure by means of bed rest and a low sodium diet

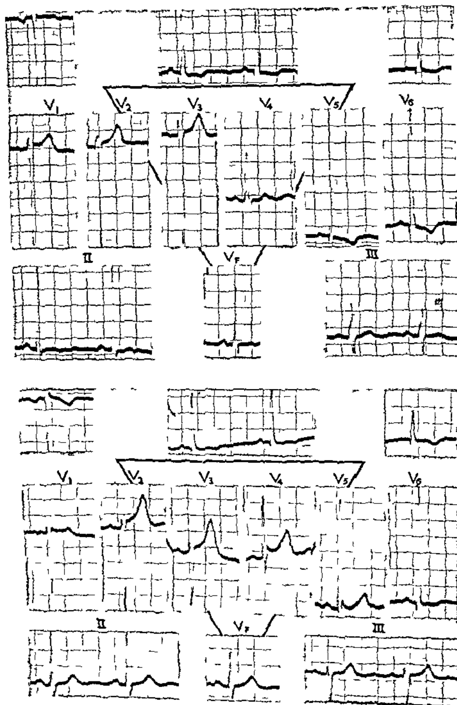


Fig 16 09—Electrocard ogram in a case of *hypertensive heart diseas* (a) before and (b) after treatment with hexa nethonium bromide and a low sod um diet Note the T wave changes *in* V₄ and V

Of the various manifestations of hypertension virtually all are relieved by combined therapy except nephrosclerosis. Headaches encephalopathy and retinopathy disappear rapidly in most instances Cerebral thrombosis is discouraged rather than encouraged by the fall in blood pressure The cerebral blood flow itself is not altered appreciably (Dewar *et al*, 1953) the cerebral vascular resistance falling more or less in proportion to the drop in blood pressure Left ventricular failure and congestive heart failure improve quickly and even some reserve can be built up in the more favourable cases (fig 16 08) Hypertensive T wave changes can be partly or wholly reversed (fig 16 09) in about half the cases (Doyle 1953) Angina pectoris is usually relieved but may be aggravated occasionally when the blood pressure falls steeply in cases with advanced coronary disease coronary thrombosis is no more common in treated than untreated cases (Doyle and Kilpatrick 1954) On effort the increased rise of blood pressure that ordinarily occurs in hypertensive subjects is suppressed (Fowler and Guz 1954)

Long term results of effectual medical treatment await the passage of the years but already it is obvious that the prognosis of malignant hypertension and hypertensive heart failure is at least twice as good as formerly Death from cerebral thrombosis, coronary thrombosis or renal failure rather than from heart failure is now the rule instead of the exception and patients live longer and in a better state of health in consequence

If treatment was undertaken much earlier at a time when it is often said to be worse than the disease the prospects might be brighter The most promising regime for early treatment is probably a combination of emotional relaxation and the rauwolfia alkaloids

While the treatment of transient hypertension cannot be considered here in detail it may be noted that toxemia of pregnancy responds very well to the low sodium diet veratrum (Assali *et al* 1950) progesterone 10 to 50 mg daily (Dalton 1954) and sympathectomy (Peat and Isberg 1949) it seems likely therefore that it should also respond to the combined treatment outlined above for essential hypertension

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that the percentage incidence of embolism is likely to appear higher in phlebothrombosis Fatal pulmonary embolism follows the injection treatment of varicose veins in 0 05 per cent of cases (Westerborn 1937) and the operative treatment in 0 4 per cent (Westerborn, 1937, McPheeters and Rice 1928)

Fractures particularly of the legs or pelvis may cause thrombo embolism on account of injury to veins immobilisation, and post traumatic acceleration of the clotting time, they may also give rise to fat embolism Malignant neoplasms especially carcinoma of the stomach may be responsible for thrombo embolism as a result of venous infiltration mechanical venous obstruction and shortening of the clotting time (owing to tissue necrosis) They may also give rise to malignant cellular emboli

The most common cause of phlebothrombosis is immobilisation in bed especially in obese subjects over 40 years of age Of 229 cases of fatal post operative pulmonary embolism Prettin (1936) found the average weight in women was 11 kg above normal and in men 4 2 kg In a series at the Mayo clinic, 93 per cent of fatal post operative pulmonary emboli occurred in patients over 40 years of age (Barnes 1937)

Congestive heart failure encourages phlebothrombo is because the circulation is slowed When the cardiac output remains elevated or is less reduced than usual as in failure from the hyperkinetic circulatory states thrombosis is rare Congestive failure due to mitral stenosis or to myocardial infarction is particularly dangerous Eppinger and Kennedy (1938) found that pulmonary embolism was the direct cause of death in 6 5 per cent of 200 fatal cases of coronary thrombosis and a contributory cause in 3 1 per cent of those with congestive failure The clotting time appears to shorten after myocardial infarction perhaps owing to the products of tissue necrosis The clotting time also appears to be shortened by digitalis (Massie *et al* 1944) and by the organic mercurial diuretics (Macht 1946) Clinically pulmonary embolism is recognised in about 10 per cent of cases with heart failure it is more frequent (20 per cent) in those with valvular disease than in those without (6 per cent) (Rissanen 1947)

Almost any major surgical procedure may result in thrombo-embolism, but abdominal and pelvic operations carry the highest embolic risk Responsible factors include post operative reduction of the clotting time (maximum at the tenth day) and immobilisation Child birth incurs a similar risk for similar reasons McCartney (1945) found that pulmonary embolism was directly responsible for 5 28 per cent of obstetrical fatalities and for 5 1 per cent of post operative deaths

HÆMODYNAMICS

Experiments in which the pulmonary arteries have been occluded in varying degree by ligature or by artificial emboli have shown that it is necessary to obstruct about 60 to 85 per cent of their total cross section before the systemic blood pressure falls or before signs of right ventricular

failure can be detected and between 85 and 100 per cent before death ensues (Haggart and Walker 1923 Gibbon Hopkinson and Churchill 1932) It is thus possible to undertake unilateral pneumonectomy without embarrassing the circulation (Barnes, 1941) In accord with these facts the majority of pulmonary emboli cause no cardiac disturbance but when a large embolus lodges at the bifurcation of the main pulmonary artery or when multiple emboli block more than two thirds of the more distal trunks the circulation is impeded and the left ventricular output falls This is the condition known as massive pulmonary embolism and implies acute obstructive pulmonary hypertension Compensatory adjustments include vasoconstriction which combats the falling blood pressure elevation of the right ventricular pressure which helps to squeeze blood past the obstruction and elevation of the venous pressure which serves to encourage the right ventricle It is as yet uncertain whether that chamber usually becomes overloaded or not In cases which recover the embolus is gradually packed to the side of the vessel where it becomes organised and finally shrinks to a mere thread Infarction of the lung does not necessarily occur because sufficient blood may pass through to nourish the tissues

Subacute cases may occur in which repeated small emboli gradually block the pulmonary circulation over a period of weeks or months (Belt 1939) There is reason to believe that secondary pulmonary vasoconstriction may develop in some cases as a reaction to this subacute obstructive pulmonary hypertension and turn a potentially reversible situation into an irreversible state that closely resembles primary pulmonary hypertension (see page 833)

Pulmonary infarction When an embolus lodges distally in a relatively small arterial trunk there is no rise of pressure in the pulmonary artery blood is not squeezed past the obstruction and the block is complete infarction of that part of the lung supplied by the occluded vessel follows (unless the collateral circulation is sufficient to nourish the ischæmic area) Of course such an event is likely to complicate massive pulmonary embolism and does so in 62 per cent of cases (Belt 1934) but it is a complication and not an essential part of the picture Admittedly experimental pulmonary embolism does not cause infarction in animals unless the circulation is otherwise impaired (Karsner and Ash 1912) but no such condition appears to be necessary in clinical medicine Infarcts of the lung are hæmorrhagic because blood from the bronchial arteries exudes into the devitalised area If this second source of nutrition is adequate for the needs of the tissue infarction does not occur When the hæmorrhagic zone reaches the surface of the lung a sero fibrinous pleural reaction develops pain may be severe as in any other pleurisy effusion is common and is usually blood stained

Pulmonary infarcts are nearly always embolic in origin (Virchow 1856) very few are due to primary pulmonary thrombosis and they rarely com

plicate idiopathic pulmonary hypertension or Fallot's tetralogy, two diseases in which primary thrombosis is relatively common

CLINICAL FEATURES

Massive pulmonary embolism In a typical dramatic attack the patient feels as if he had been struck in the centre of the chest and rapidly becomes faint, grey, cold, clammy and breathless Central sternal pain may be indistinguishable from that of acute myocardial infarction Consciousness may be lost Peripheral cyanosis is evident in the ears lips and nail beds but

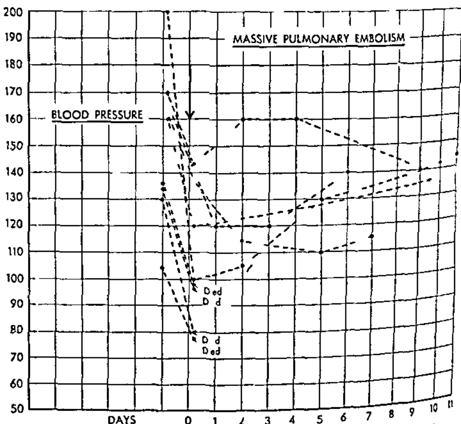


Fig 17 01—Behaviour of the blood pressure in 9 cases of massive pulmonary embolism. There is invariably a profound initial drop In the group shown those with relatively high blood pressures previously recovered whereas those with relatively low pressures previously died

elsewhere pallor is usually more noticeable Sweating is commonly profuse The pulse is thready and rapid, or may be imperceptible the blood pressure is low or immeasurable (fig 17 01) The jugular venous pressure is invariably raised (fig 17 02) and the liver may be palpable cardiac œdema is not seen in acute cases but may occur later in the subacute form Examination of the lungs may reveal nothing abnormal The heart sounds are usually soft, although the second sound at the base may be relatively accentuated

or widely split (if there is right bundle branch block) Clinical and direct visual evidence of dilatation of the pulmonary artery proximal to the embolus have been described by McGinn and White (1935) and by Churchill (1934) respectively The Graham Steele murmur of functional pulmonary incompetence has been heard (White and Brenner 1933) Occasionally a pericardial friction rub develops over the base of the distended pulmonary artery (White 1937)

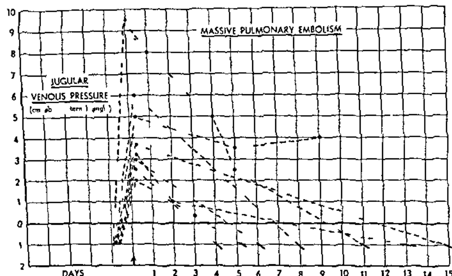


Fig 17 02—Behaviour of the venous pressure in 8 cases of massive pulmonary embolism There is initial elevation in all but it is rarely maintained for more than a few days

Rarely patients die abruptly at the onset presumably from reflex cardiac inhibition or ventricular fibrillation such deaths being preventable by atropine in animals and being independent of the size of the embolus (Scherf and Schonbrunner 1937) The great majority however survive the initial insult but about one third die subsequently from circulatory obstruction approximately 10 per cent within 10 minutes 30 per cent within an hour and 60 per cent in a matter of hours or days (de Takats and Fowler 1945) On the other hand about two thirds recover—within hours days or weeks Throughout this anxious period there is a 25 per cent risk of another and perhaps fatal embolus

Massive pulmonary embolism however is not always dramatic and mild cases are easily overlooked Passing tightness of the chest fleeting unexplained breathlessness transient faintness or a symptomless rise of systemic venous pressure may be the sole manifestation of an event that brought death very close

Subacute cases may pass gradually into congestive heart failure wi

a single incident suggesting embolism the clinical features of these rare cases resemble those of primary pulmonary hypertension

It should be noted that calling for the bed pan and falling back dead is not specially correlated with pulmonary embolism The phenomenon appears to be associated with impending death from ventricular fibrillation

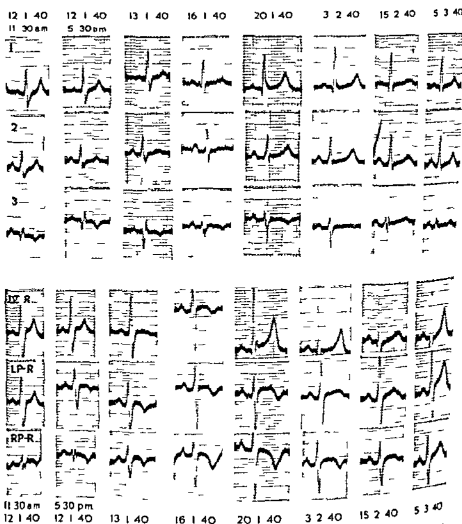


Fig 17 03—*Electrocardiogram showing the characteristic appearances associated with massive pulmonary embolism* (lead IV R—CR4 LP R—CR2 3 RP R=CR1)

or asystole, and may occur as a tragic climax to many *forms* of heart disease including aortic stenosis and myocardial infarction The colonic disturbance may be a vagal manifestation Abrupt death from pulmonary embolism, preceded or not by a call to stool is rare as already mentioned

The diagnosis of acute right ventricular stress may be proved electrocardiographically (fig 17 03) Limb leads show sinus *tachycardia* a con

stant S wave in lead 1 a frequent Q wave in lead 3 inversion of T_3 flattening or slight inversion of T and rather low voltage (Barnes 1937) Occasionally P becomes tall and sharp (Wood 1948) These appearances are not unlike those of posterior myocardial infarction although an absent S_1 conspicuous Q and elevation of the R T segment in lead 3 should be sufficient to distinguish the latter in standard leads Again, Q_3 in cases of massive pulmonary embolism is caused by cardiac rotation, and is not seen

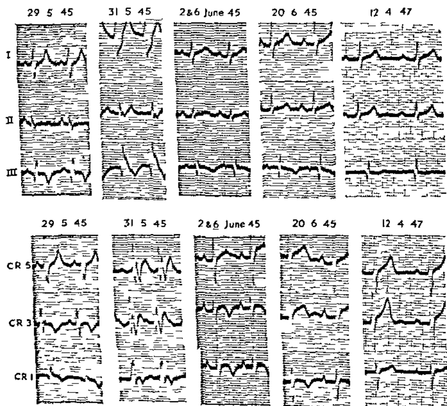


Fig 17 04—Electrocardiogram showing transient right bundle branch block in a case of massive pulmonary embolism

in lead V_F In multiple chest leads appearances are equally characteristic (Wood 1941) the T wave is nearly always inverted in leads V_{1-3} over the right ventricle sometimes in V_4 and occasionally even in V (fig 17 03) and clockwise rotation or displacement of the interventricular septum to the left brings the RS pattern round as far as V_5 or even V_6 There are no pathological Q waves and the RS T segment is not deviated from the base line but in about 15 per cent of cases there is transient right bundle branch block (fig 17 04) These changes are not immediate but develop within a few hours and are usually maximum within one to three days Rec

should be made for the source As previously stated this is commonly phlebothrombosis in the legs It usually begins in the calf where there may be deep muscle tenderness, or pain on dorsiflexing the foot (Homans sign) If a pressure cuff is wrapped round the thigh and inflated to 40 mm Hg a characteristic pain develops in the calf when there is phlebothrombosis (Ortiz Ramirez and Serna Ramirez 1955) Superficial thrombosis in the long saphenous vein may be felt as a solid cord and is usually tender With thrombophlebitis the overlying skin is hot red indurated and painful Extension to the femoral vein causes a conspicuous rise of skin temperature in the affected limb a most useful sign of serious phlebo thrombosis œdema also occurs in many cases but is less constant

PROGNOSIS

It is not easy to assess the true mortality rate in thrombo embolism for many mild cases are overlooked, but in a consecutive series of twenty clinically recognised cases of massive pulmonary embolism seen by the author six died In necropsy material, about two thirds of all pulmonary emboli are major involving more than 50 per cent of the cross section of the pulmonary arteries (Belt 1939) but it is naturally the more severe ones that are seen at necropsy From evidence of this kind it is estimated that nearly two thirds of all cases of massive pulmonary embolism recover and that less than a third of clinical thrombo emboli are massive this gives a total mortality rate of about 10 per cent In those that recover there are ordinarily no sequelæ but there is an important though small group of cases in which subacute obstructive pulmonary hypertension leads to permanent and finally fatal chronic pulmonary hypertension

TREATMENT

Prophylaxis is most important and should be directed towards accelerat ing the venous circulation in the legs and preventing the clotting process in bed ridden patients

Breathing exercises frequent changes of position, active movements of the legs for specified times every day prevention of dehydration and limitation of morphine are simple logical and effective measures Heart failure should be treated quickly and adequately Rest in bed should never be prolonged unnecessarily

Heparin is the quickest and safest anticoagulant but it is too expensive for routine prophylactic use It should certainly be employed however as soon as phlebothrombosis or thrombo embolism is recognised for 23 per cent are multiple (Nygaard *et al* 1940–41) and not more than a quarter of cases of massive pulmonary embolism are fatal at the first insult (de Takats and Fowler, 1945) Heparin may be given intravenously in doses of 50 mg (5 000 units) four to six hourly by continuous intravenous drip in doses of 150 to 300 mg daily (50 to 100 mg to a pint of normal saline) or intra

muscularly or subcutaneously combined with 2 ml of 2 per cent procaine in doses of 150 mg twice daily The last route is simple and effective Procaine prevents pain and local bruising is rarely serious The dose of heparin should be regulated so that the clotting time is maintained at about two to three times the normal (Murray and Best 1938) Pitkin s menstruum (gelatin 18 per cent dextrose 8 per cent glacial acetic acid 0 5 per cent distilled water to 100 per cent) as a vehicle for heparin to retard its absorption (Loewe *et al* 1946) is usually too painful for routine use

In the event of hæmorrhage the anticoagulant effects of 5 000 units (50 mg) of heparin may be neutralised immediately by injecting 50 mg of protamine sulphate intravenously (Parkin and Kvale 1949)

Heparin is the sulphuric ester of a complex polysaccharide (Jorpes and Bergstrom 1937) and in view of the difficulty in preparing it from liver and therefore its expense strenuous efforts were made to find a sulphuric ester of some other polysaccharide that could be used as a substitute This search was rewarded by the discovery that several such esters had powerful anticoagulant properties including paritol (Sorenson and Wright 1950) treburon (Field *et al* 1953) and dextran sulphate (Ricketts *et al* 1953) The most promising and least toxic of these appears to be dextran sulphate Weight for weight paritol is one seventh as potent as heparin but its anticoagulant effect lasts two to three times longer treburon is one third as potent as heparin but lasts one and a half times longer dextran sulphate is put up in units that are equivalent to heparin but its effects last two to three times longer Paritol may cause swelling of the hands and feet and serious vasomotor collapse treburon has been reported to produce severe diarrhœa and late alopecia in some cases but has the advantage of being painless when injected intramuscularly dextran sulphate appears to be non toxic The heparin like action of dextran sulphate includes its ability to clear the turbidity of lipid laden plasma (Brown 1952) Its chief dis advantage is that it can only be given intravenously

Dicoumarol (3 3 Methylene bis 4 hydroxycoumarin) the cause of hæmorrhagic sweet clover disease of cattle (Link 1943) is a cheap and effective anticoagulant but its action is delayed for forty eight to seventy two hours and is cumulative so that it is difficult to control It acts indirectly by preventing the liver from manufacturing prothrombin Dicoumarol is *given by mouth in single doses each day* beginning with 300 mg the first day 200 mg the second and 100 mg the third sub sequent doses (usually 50 to 100 mg) being adjusted according to the prothrombin time which should be kept as close as possible to two and a half times the prothrombin time in a normal control i e at a patient/control prothrombin ratio of 2 5 usually achieved with a maintenance dose of 50 to 100 mg daily In the past this ratio has been expressed reciprocally as an index i e $\frac{\text{control time}}{\text{patient s time}} \times 100$ or 40 per cent for a ratio of 2 5 T means that with a control time of 12 seconds, the patient s

time should be kept at 30 seconds The prothrombin time is inversely proportional to the prothrombin content of the plasma If the former is measured with increasing dilutions of plasma a graph may be constructed by plotting the prothrombin times against the respective plasma dilutions (or their reciprocals if the graph is to be a straight line instead of an impracticable rectangular hyperbola) If the patient s prothrombin time is read off on such a graph (constructed for normal plasma) it may be expressed in terms of prothrombin activity or content No practical advantage is gained by this manœuvre which has been the source of much confusion where there is no room for any misunderstanding whatsoever In fact a prothrombin ratio of 2 5 or index of 40 per cent is usually equivalent to an activity or content of 15 to 20 per cent It is solely to avoid any possibility of error that experienced physicians often prefer to chart the prothrombin time itself in seconds and to record the control time separately below

At first the prothrombin time should be measured daily, but as soon as the graph stabilises it may be estimated less frequently e g every second day then twice weekly, and finally once a week Frequent adjustments of the daily dose of dicoumarol are usually necessary at first but after a while it is easier to judge the right maintenance dose About 10 per cent of individuals are unduly sensitive to dicoumarol and an equal number unduly resistant the degree of sensitivity or resistance seems to be determined by heredity and changes little over the years

If the prothrombin ratio exceeds 3 microscopic hæmaturia may occur and if it exceeds 3 5 to 4 hæmorrhage may be serious or even fatal Hæmaturia malena and purpura occur in that order of frequency but a fatal hæmorrhage may be cerebral pericardial or retro peritoneal With proper laboratory control however, clinical hæmorrhage is rare (1 per cent) and a safe level of prothrombin activity can be restored immediately by blood transfusion or within a few hours by injecting 200 mg of vitamin K_1 intravenously (Douglas and Brown 1952) It has since been shown that 25 to 50 mg of vitamin K_1 orally is usually quite sufficient to restore normal prothrombin times and 15 to 25 mg to restore a satisfactory blood therapeutic level of prothrombin when it is desired to continue dicoumarol therapy (Toohey 1954) In the event of serious hæmorrhage *it is* hardly necessary to add that dicoumarol must be withheld at once whatever the prothrombin time for bleeds have been reported occasionally when the prothrombin activity has been well within the desired therapeutic range

When all goes well treatment should be continued for at least three weeks and preferably for six weeks in all cases of thrombo embolism and there should be no hesitation in continuing for three to six months in cases giving a history of recurrent thrombo embolic episodes

In view of the delayed effect of dicoumarol, heparin is usually given as well during the first forty eight to seventy two hours With this treatment the post operative mortality rate from massive pulmonary embolism in

cases specially selected as thrombo embolic risks has been reduced from perhaps 5 per cent to 0 1 to 1 0 per cent (Barker *et al* 1945 Wright 1946)

Many other coumarin derivatives have been shown to act like dicoumarol and have been used clinically as anticoagulants Some of them such as marcoumar [3 (1 phenyl propyl) 4 hydroxycoumarin] are even longer lasting and more cumulative than dicoumarol and therefore have little to recommend them for this property is a disadvantage Cyclocumarol (cumopyran) is in the same category Marcoumar, for example inhibits the manufacture of prothrombin for five days after a single dose Weight for weight it is very powerful the loading dose being 21 9 and 3 mg at daily intervals and the maintenance dose around 3 mg daily (Bourgain *et al*, 1954)

Ethyl biscoumacetate [bis 3 3 (4 oxycoumarinyl) ethyl acetate] introduced as tromexan and pelentan, is in a different class for its maximum effect occurs between eight and twenty four hours after a single dose and the prothrombin time returns to normal within the next eight to twenty four hours according to the size of the dose (Burt Wright and Kubik 1949) Being three to four times less active than dicoumarol the initial loading dose is high usually 900 600 and 300 mg at daily intervals, whilst the maintenance dose is commonly 300 to 600 mg daily it is also best given in divided doses two or three times daily (a tablet contains 300 mg) Ethyl biscoumacetate however is expensive and has been largely replaced by dindevan

Sinthrone, which is 3 [α (4′ nitrophenyl)β acetyl ethyl] 4 oxycoumarin is probably the best of the coumarin derivatives for clinical purposes in that a therapeutic level of reduced prothrombin activity can be achieved easily in twenty four to forty-eight hours and maintained steadily on a small daily maintenance dose whilst there is little cumulative effect The loading do e is 24 mg the first day 16 mg the second and 4 to 8 mg thereafter according to the prothrombin ratio (Moeschlin and Schorno 1955) Sinthrome is put up in 4 mg tablets

Phenylindanedione (2 phenylindane 1 3 dione) or dindevan appears to approach the ideal therapeutic drug of its class and is the most active prothrombopenic agent of the indanedione derivatives (Soulier and Gueguen 1947 1948) moreover it is much cheaper than tromexan Its effect on the prothrombin time is maximum between twenty four and thirty six hours after a single dose and it has virtually no effect after forty eight hours (Toohey 1953) Given in divided doses twice daily it therefore keeps the prothrombin level steadier than tromexan on the other hand its relatively short period of activity, and the absence of a cumulative effect make it much safer and easier to manage than dicoumarol Phenindione as it is now being called is non toxic but dermatitis apparently due to the development of hypersensitivity to the drug developed in two of my own cases The loading dose is 150 to 200 mg on the first day 100 mg on the second and 50 mg on the morning of

third for maintenance 50 to 150 mg daily is usual Tablets contain 50 mg but are scored so that 25 mg doses may be given

Hæmorrhages are rare with the shorter acting prothrombin depressors and relatively small doses of vitamin K_1 (10 to 15 mg orally or 5 mg intravenously) are usually sufficient to restore safe prothrombin levels within twenty four hours if an overdose has been given (Toohey 1954 Dawson 1955) Nevertheless it must never be forgotten that all anticoagulants are potentially dangerous and should not be given lightly or without proper laboratory facilities nor should they be given to any patient with an active peptic ulcer or with a recent history of spontaneous hæmorrhage from any source They should be withheld temporarily in the event of any surgical operation dental extraction or infective hepatitis

Bilateral ligation of the femoral or common iliac veins or ligation of the inferior vena cava has been received with less enthusiasm but it may be a life saving procedure when anti coagulants are contraindicated Subsequent œdema when present, usually passes off within three months and little detrimental clinical or physiological effects can be detected as a rule (Burch and Ray 1947) Recurrent superficial thrombophlebitis however may prove troublesome

Treatment of acute obstructive pulmonary hypertension

Relatively mild cases recover spontaneously and require no special treatment The majority of those clinically recognised however are seriously ill and require urgent attention The objective is very simple it is to keep the patient alive long enough for the clot to retract and so relieve the obstruction at the same time further emboli must be prevented at all costs To this end the following procedures should be carried out immediately

1 The patient should be nursed flat in order to encourage the cerebral circulation Warmth should not be applied to the body and vasodilating agents should not be given with the idea of dilating the pulmonary artery for these merely serve to lower the blood pressure which is already critically reduced and can have no influence on the large pulmonary vessels

2 Oxygen should be given through a light plastic mask or the patient may be nursed in an oxygen tent so that the litre or two of blood that is passing through the lungs may be supersaturated with oxygen

3 The basal vasomotor and respiratory centres must be supported for their collapse means instant death For this purpose nikethamide (coramine) has no equal and it should be given in doses of at least 0 5 to 1 G (2 to 4 ml of the standard 25 per cent solution) intravenously as often as required (even every five minutes in desperate situations) and if there is no response to 1 G the dose should be doubled Nikethamide is rapidly inactivated in the blood stream and there is therefore no danger of a cumulative effect An overdose however may give rise to convulsions

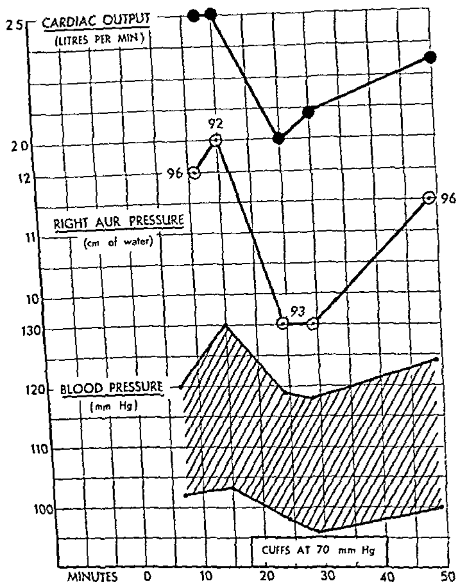


Fig 17 06—Effect of a venous pressure lowering agent (cuffs on the thighs) on the blood pressure and cardiac output of a case of massi e pulmonary embolism

Morphine is contra-indicated in view of its depressing effect on respiration, and pethidine is also better withheld in view of its vasodilating action at least until the situation is under control

4 The blood pressure must be maintained by means of noradrenaline aramine or mephentermine (wyamine), as described on page 749

5 Heparin 10 000 to 15 000 units should be given intravenously at once, and repeated in doses of 5 000 to 10 000 units four to six hourly during the first forty eight hours As soon as the patient is able to swallow 200 mg of phenylindanedione should be given followed by 100 mg the following day subsequent doses being regulated according to the prothrombin ratio Anticoagulant treatment must be maintained at a high therapeutic level (ratio nearer 3 than 2) for at least three weeks, or until the danger of recurrent embolism is passed

6 Ouabain or digoxin 1 mg may be given intravenously if the venous pressure is more than 5 cm above the sternal angle at 30 degrees on the chance that the right ventricle is overloaded and 0 5 mg doses may be repeated twice at six hourly intervals In a typical case of the author s however lowering the venous pressure resulted in a fall of cardiac output and blood pressure (fig 17 06) suggesting that the right ventricle was not overloaded

The Trendelenburg operation (Trendelenburg 1908)—exposure of the pulmonary artery and removal of the clot—is only possible if a well trained and thoroughly prepared surgical team is available and is only practised when the situation is desperate the operative mortality is over 90 per cent (Nygaard 1938) and spontaneous recovery is the rule rather than the exception The first successful embolectomy in *Great Britain* was reported by Ivor Lewis in 1939

Treatment of pulmonary infarction No specific treatment is required for pulmonary infarction itself but secondary infection or septic embolism calls for penicillin or other suitable antibiotic, morphine may be necessary if there is severe pleural pain and hæmorrhagic pleural effusion may need aspirating if extensive Infarction does not contraindicate anticoagulants

PARADOXICAL EMBOLISM

Valvular patency of the foramen ovale is present in about a third of all individuals but the opening remains closed because the pressure in the left atrium is higher than that in the right When the right ventricle fails however the atrial pressures may be reversed the valve then opens and blood is shunted from right to left This event is improbable in heart failure secondary to mitral stenosis for the left atrial pressure remains too high Ideal conditions are presented by acute right ventricular failure due to massive pulmonary embolism for not only is the right atrial pressure then raised but the left is lowered as in pulmonary stenosis, and emboli are

already forthcoming Having passed through the foramen ovale the embolus is carried into the systemic circulation and may lodge in any cerebral visceral or peripheral artery

AIR EMBOLISM

Small quantities of air may be injected into the systemic venous system of healthy subjects with little risk indeed about 15 ml per kg body weight are required to kill a dog even when injected rapidly (Wolffe and Robertson 1935) Fatalities have occurred however when air has been accidentally introduced into a vein during an operation intravenous infusion therapeutic or diagnostic procedure The clinical features are those of massive pulmonary embolism but in addition a loud churning sound or millwheel murmur may be heard over the right ventricle and pulmonary artery Death appears to result from circulatory obstruction due to air lock in the outflow tract of the right ventricle Treatment consists of turning the patient into the left lateral position in the hope of displacing the air into the right atrium (Oppenheimer Durant and Lynch 1953) A similar manœuvre has proved life saving in dogs but has not yet been tried in man

FAT EMBOLISM

Globules of fat may penetrate the systemic venous circulation following fractures usually of the femur and accidents have occasionally occurred during therapeutic or diagnostic procedures involving the use of oil Fat embolism has several characteristics which help to distinguish it from other forms First it happens within a few hours of the accident perhaps while manipulating the injured limb under anæsthesia or when moving the patient to the X ray department Second signs of multiple systemic embolism usually complicate the picture owing to the passage of fat globules through the pulmonary capillaries Thus there may be severe headache drowsiness or loss of consciousness usually without localising signs multiple petechial spots may appear in the skin red cells albumin and droplets of oil may be found in the urine Third breathlessness and cyanosis are associated with the development of fine crepitations over all areas of the lungs and skiagrams show an abundance of cotton wool shadows in all zones The mortality rate is similar to that of other forms of massive pulmonary embolism but those who survive recover remarkably quickly – often within forty eight hours

EMBOLISM DUE TO FOREIGN BODY

Metallic fragments from gun shot wounds and even bullets may enter the circulation in rare instances Such an event should be considered if a skiagram shows an intra thoracic foreign body when there is no wound of the chest or adjacent structures An intravascular metallic foreign body may remain mobile for several days and may move against the bloodstream if so directed by the force of gravity Surgical attempts to remove

missile may be foiled by such behaviour An excellent example was described by Bauer (1943)

MALIGNANT EMBOLI

Cancer cells may infiltrate the systemic venous system and be swept into the lungs in the form of cellular emboli Subacute pulmonary hyper



17 07—Skiagram showing miliary embolic carcinomatosis of the lungs



Fig 17 08—Radiological appearances of the lungs showing embolic secondaries due to chorionepithelioma

(B t y f D Pl ll p Film

tension develops if more than two thirds of the vessels are blocked the clinical features resembling those of massive pulmonary embolism but with an insidious onset and progressive course The diagnosis may be suggested by the skiagram which may show minute miliary lesions (fig 17 07) Cases so far reported have been due either to carcinoma of the stomach (Brill and Robertson 1937) or breast (Mason 1940) or to chorionepithelioma (fig 17 08)

Subacute pulmonary hypertension may also be due to multiple pulmonary thromboses secondary to perivascular lymphatic carcinomatous infiltration (Brill and Robertson 1937) As a rule however, these cases present with subacute hypoxic cor pulmonale (q v)

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Fig 17 07—Skiagram showing miliary embolic carcinomatosis of the lungs



Fig 17 08—Radiological appearances of the lungs showing embolic secondaries due to chorionepithelioma

(B ... J D Phillip Ellman)

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CHAPTER XVIII

PULMONARY HYPERTENSION

Normal pulmonary blood pressure

The average normal pulmonary blood pressure is 16/7 mm Hg (mean 11 mm Hg) with reference to the sternal angle This figure is based on fifty normal controls investigated by the author for one reason or another over the past eight years The cardiac output at the time ranged between 5 8 and 12 8 litres per minute (average 8 6) As repeatedly pointed out conditions are not basal during cardiac catheterisation The normal mean *left atrial pressure averages 2 to 3 mm Hg above the sternal angle* so that the normal pulmonary artery-left atrial pressure gradient is 8 to 9 mm Hg and the pulmonary vascular resistance (page 177 is therefore $\frac{8 \text{ to } 9}{8\ 6}$ or around unity (80 dynes sec/cm ^{5}) Conventional figures are 10 mm Hg for the gradient 5 litres per minute for the cardiac output and 2 units for the resistance

Definition and classification of pulmonary hypertension

Pulmonary hypertension literally implies a pulmonary blood pressure above 30/15 mm Hg which is the upper limit of the normal range Physiologically there are four entirely different mechanisms that may produce pulmonary hypertension namely appreciable elevation of the left atrial pressure obstruction or obliteration of more than two thirds of the total cross section of the pulmonary vascular bed at any level a sufficiently increased pulmonary blood flow and active pulmonary vaso constriction each of these mechanisms causes its own particular variety of pulmonary hypertension which may be labelled respectively passive obstructive or obliterative hyperkinetic and vasoconstrictive *There is* no doubt that any form of pulmonary hypertension if sufficiently severe and prolonged finally produces sclerotic changes in the pulmonary arteries with or without local thromboses which may add an obliterative or obstructive element to the picture and there is good reason to suspect that any form of pronounced pulmonary hypertension may also excite a vasoconstrictive reaction and so turn passive obstructive or hyperkinetic pulmonary hypertension into the more serious vasoconstrictive type Such a reaction would close a vicious circle and so transform a relatively innocent pulmonary hypertension into a more or less malignant form The parallel between this hypothesis and current theory in respect of systemic hyper tension will not pass unnoticed

PASSIVE PULMONARY HYPERTENSION

Mean left atrial pressures of 20 to 30 mm Hg at rest and 40 to 50 mm Hg on effort are common in mitral stenosis In such cases the mean pulmonary artery pressure must be at least 10 mm Hg higher if the normal pressure gradient is to be preserved A similar situation arises in mitral incompetence and left ventricular failure This may be called passive pulmonary hypertension because it represents no more than transmitted pulmonary venous hypertension Left atrial pressures of 15 to 20 mm Hg and therefore mean pulmonary artery pressures of 25 to 30 mm Hg are usual in chronic constrictive pericarditis and in cases of congestive heart failure due to any generalised cardiopathy such as isolated myocarditis but they do not rise on effort because the right ventricle is incapable of increasing its stroke output Passive pulmonary hypertension in these cases is therefore trivial

Reactive pulmonary vasoconstriction raised the pulmonary vascular resistance to between 6 and 10 units in 16 per cent of 275 critical cases of mitral stenosis studied by the author and to over 10 units (average 17) in 12 per cent By critical is meant sufficient stenosis (orifice around 1×0 5 cm) to raise the left atrial pressure 20 mm Hg or more when the cardiac output is 4 to 5 litres per minute and the heart rate normal i e sufficient to cause a mean pulmonary artery pressure over 30 mm Hg at rest Reactive pulmonary vasoconstriction does not seem to occur in response to less passive pulmonary hypertension than this Whether it is persistent pulmonary hypertension of the order of 50/25 mm Hg or repetitive pulmonary hypertension of a much higher degree that is responsible for the vasoconstrictive reaction is unknown indeed, there is no direct proof that it is the pulmonary hypertension that is causing the vasoconstrictive reaction at all Certainly the historical and objective lack of chronic interstitial œdema of the lungs in cases with an extreme resistance exonerate that factor as a possible etiological agent

The incidence of active pulmonary vasoconstriction in mitral incompetence appears to be lower Of 58 cases severe enough to have warranted mitral valve repair had such an operation been available only 14 per cent had an appreciably increased pulmonary vascular resistance (9 per cent between 6 and 10 units and 5 per cent in the extreme range over 10 units) The lower *mean* left atrial pressure and lower mean level of passive pulmonary hypertension may explain this lower incidence of the vasoconstrictive response Alternatively the factor that seems to limit right ventricular filling in severe mitral incompetence (Bernheim effect or increased pericardial tension?) may prevent surges of right ventricular output and undue rises of pressure on effort Certainly an increased pulmonary venous or arterial pulse pressure which is characteristic of mitral incompetence cannot be responsible for reactive vasoconstriction or the latter would be more common in mitral incompetence than

No figures are available for the frequency of active pulmonary hypertension secondary to the passive pulmonary hypertension of left ventricular failure It was observed on page 774 however, that many cases that present clinically with the Bernheim syndrome prove to be examples of right ventricular failure secondary to reactive pulmonary vasoconstriction

No instance of extreme pulmonary vasoconstriction has yet been recorded secondary to the relatively mild passive pulmonary hypertension of Pick s disease and generalised cardiopathies This again suggests that a critical level of pulmonary hypertension must be reached before significant reactive vasoconstriction occurs

The clinical details of passive pulmonary hypertension and its vasoconstrictive response (Wood 1954) have already been discussed in relation to mitral valve disease on page 540 and to left ventricular failure on page 774

HYPERKINETIC PULMONARY HYPERTENSION

As the blood flow through the lungs increases the vessels dilate to accommodate the extra volume and temporarily closed vessels probably open up so that the resistance falls there is thus little or no rise of pressure at first (Hickam and Cargill 1947 Riley *et al*, 1948) but as the flow approaches three times the normal (15 litres per minute in an adult of average height and weight) a state of maximum vasodilatation is reached and no further drop in resistance is possible thereafter the pulmonary blood pressure rises in proportion to the flow (Cournand 1950) In other cases the pulmonary vascular resistance does not alter much with effort the pulmonary blood pressure tending to rise with quite small changes of output (Dexter *et al* 1951 Donald *et al*, 1955) In disease both types of response are seen For example pulmonary blood flows of 10 to 15 litres per minute reduced resistance and no appreciable rise of pulmonary blood pressure are characteristic of many cases of atrial septal defect in the majority of cases of patent ductus or ventricular septal defect on the other hand flows of this order are usually associated with some rise of pressure the resistance being normal (or even slightly raised) rather than unduly low With flows of 20 to 30 litres per minute the pulmonary blood pressure may approach and even reach systemic level Hyperkinetic pulmonary hypertension then may be defined as a raised pulmonary blood pressure associated with an increased flow and normal resistance

In the generalised hyperkinetic circulatory states such as thyrotoxicosis beri beri Paget s disease of bone anæmia, cor pulmonale hepatic failure pregnancy and phæochromocytoma of the adrenaline (rather than nor adrenaline) type the frequency of hyperkinetic pulmonary hypertension is not yet known, but there can be little doubt that it may occur, especially perhaps in beri beri The increased pulmonary blood flow in cor pulmonale is particularly important because it may be associated with some degree

of obliterative pulmonary hypertension and the combination may be responsible for very high pulmonary blood pressures

Of the congenital shunts there are at least five acyanotic and five cyanotic forms that may result in hyperkinetic pulmonary hypertension

Acyanotic	*Cyanotic*
Partial anomalous pulmonary venous drainage	Total anomalous pulmonary venous drainage
Atrial septal defect	Single atrium
Ventricular septal defect	Single ventricle
Patent ductus arteriosus	Persistent truncus
Aorto pulmonary septal defect	Transposition of the great vessels

These have all been discussed in detail in the chapter on congenital heart disease

Appreciable reactive pulmonary vasoconstriction occurred in one quarter of a consecutive series of 100 critical cases of atrial septal defect and two thirds of 100 critical cases of patent ductus or ventricular septal defect studied by the author By critical is meant a defect of sufficient size to cause a pulmonary blood flow of at least three times the systemic flow in the presence of a normal pulmonary vascular resistance Clinically this means that the case would be regarded as severe or gross rather than mild or moderate in degree (In the 93 cases that had developed the vasoconstrictive response the pulmonary vascular resistance lay between 6 and 10 units in 29 and between 10 and 30 units (average 17) in 64 This suggests that if the reaction occurs at all it is likely to become extreme The presence or absence of the vasoconstrictive response was obviously determined at birth in the great majority if not in all cases and the idea that pulmonary hypertension due to a high pulmonary vascular resistance develops slowly over the years is totally unsupported by all available data Obstructive pulmonary hypertension due to embolism or thrombosis may occur suddenly in the later stages of these diseases but that is another matter altogether The evidence suggests that in one group of individuals hyperkinetic pulmonary hypertension at once causes persistent pulmonary vasoconstriction whereas in another group of individuals it does not The secret of this difference in behaviour has not yet been discovered nor is it yet understood why cases of atrial septal defect are less likely to develop the reaction than cases of patent ductus and ventricular septal defect of comparable severity

The clinical features of hyperkinetic pulmonary hypertension and the effect of the vasoconstrictive reaction on the physiology of the circulation in all these congenital anomalies have already been described in Chapter VIII and cannot be further considered here

OBSTRUCTIVE OR OBLITERATIVE PULMONARY HYPERTENSION

The word obstructive is best applied to massive pulmonary embolism or thrombosis and to subacute miliary thrombo embolism or widespread peripheral pulmonary thromboses pneumonectomy also provides an example of artificial obstruction of half the total cross section of the pulmonary vascular tree Carcinomatous embolism and diffuse infiltrative lymphatic carcinomatosis behave rather differently and will be described as a form of subacute cor pulmonale in Chapter XIX although secondary widespread thromboses may also cause obstructive pulmonary hypertension The term obliterative more accurately describes the situation in respect of the capillaries in emphysema and the small arteries and arterioles when they are partially or wholly blocked by gross endocardial thickening as an anatomical reaction to severe and prolonged pulmonary hypertension of any kind, secondary to subacute thrombo embolism or as a result of certain forms of arteritis including periarteritis nodosa disseminated lupus and schistosomiasis Secondary thrombosis is common in these partially occluded vessels so that obstructive and obliterative types may overlap

Massive pulmonary embolism was considered fully in the last chapter

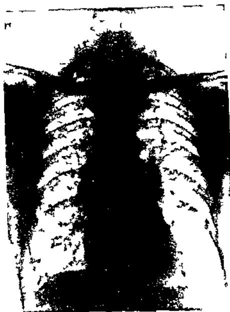
Massive pulmonary thrombosis is relatively rare but may complicate any form of long standing pulmonary hypertension that has developed extensive pulmonary atherosclerosis Its pathogenesis is comparable to thrombosis at the distal end of the descending aorta in elderly men with gross aortic atherosclerosis

The degree of obstructive pulmonary hypertension produced obviously depends on the size and number of vessels thrombosed As a rule *only one* major vessel is involved, and even if this is the main right or left pulmonary artery not more than half the total cross section of the pulmonary arterial tree is cut off and therefore pulmonary hypertension would not arise if the rest of the circulation were normal But the pulmonary circulation is never normal in these cases for otherwise neither the atherosclerosis nor the secondary thrombosis would occur The complication therefore nearly always has serious consequences In the congenital group with hyperkinetic pulmonary hypertension massive thrombosis may greatly elevate the pulmonary blood pressure overload the right ventricle and reverse the shunt In obliterative or vasoconstrictive pulmonary hypertension the relatively sudden increase of total pulmonary vascular resistance usually causes immediate right ventricular failure

Clinically massive thrombosis should be suspected in any advanced case of pulmonary hypertension of any type if there is relatively sudden deterioration in effort tolerance unexpected shunt reversal or unexpected heart failure Pulmonary thrombosis is never a dramatic event *like* massive pulmonary embolism and deterioration may be quite insidious in some cases As a rule the breakdown associated with thrombosis is subacute

rather than acute or chronic and the majority of cases are fatal (Magidson and Jacobson 1955)

The diagnosis may be confirmed by the skiagram which may show an exceptionally dense bulky pulseless comma shaped shadow in the position of one or other main pulmonary artery (fig 18 01) and an unduly translucent ischæmic lung distal to the block on one or other side (Keating *et al* 1953) Proof of the obstruction may be obtained by means of angio cardiography but this is rarely necessary





(a) 22nd March 1944 (b) 5th December 1946

Fig 18 01—Development of thrombosis of the right pulmonary artery in a case of anoxic cor pulmonale

Subacute thrombo embolic pulmonary hypertension

This is one of the most important forms of severe pulmonary hyper tension for several reasons (1) socially and economically because it most commonly affects otherwise healthy young married women after childbirth (2) therapeutically because it can be cured by swift diagnosis and adequate treatment but is otherwise fatal (3) experimentally because it can be wholly reproduced and investigated in animal (4) academically because it is a most important and thoroughly understood link between simple obstructive pulmonary hypertension secondary obliterative pulmonary hypertension and so called primary pulmonary hypertension (*vide infra*) The disease therefore repays close scrutiny

Experimentally the condition has been reproduced in rabbits by repeated intravenous injection of finely fragmented fibrin clot

relatively large doses the rabbits died from heart failure secondary to obstructive pulmonary hypertension When the dose was nicely judged for the purpose however, the rabbits lived longer the emboli became organised, the lumens of the obstructed small arteries were reconstituted and the vessels were left with marked fibro elastic intimal thickening which was indistinguishable from that seen in primary pulmonary hypertension (Harrison 1948) This important work was confirmed by Barnard (1954) who produced similar lesions of the small arteries and arterioles of mice and rabbits by injecting thromboplastin into the systemic venous system so that fibrin emboli were formed *in vivo*

Physiologically pulmonary hypertension is initially obstructive then obliterative and finally may well be vasoconstrictive in response to the hypertension itself

Clinically cases present in a subacute manner with right ventricular failure secondary to severe pulmonary hypertension The majority are young married women and symptoms develop soon after childbirth occasionally the condition arises during pregnancy or is associated with some other cause of recurrent intravascular clotting of the appropriate kind Thus one of my five cases occurred in a young man following a sprained ankle small emboli being liberated from repeated phlebo thrombosis in the vicinity Death occurred within six months from right ventricular failure secondary to severe pulmonary hypertension Repeated small hæmoptyses were a feature of this case Of the other four two (a woman aged 40 and a man aged 36) followed simple recurrent thrombo phlebitis in the legs one of them died after a typical course lasting 18 months and the other is still alive on permanent anticoagulant treat ment The other two aged 27 and 25 were both associated with phlebo thrombosis following pregnancy One of them who appeared to be dying with advanced heart failure after inadequate treatment for two to three months was cured by prolonged anticoagulant therapy strict bed rest and intensive treatment for heart failure over a period of three months Final catheterisation in her case revealed complete restoration of the pulmonary vascular resistance to normal The other was progressing favourably with similar treatment for six weeks when she discharged herself from hospital because her husband did not appear to believe that she was seriously ill and needed her services at home At this time her pulmonary vascular resistance had fallen to 5 3 units (P A P 50/13 mm Hg C O 5 1 L/min) and she had improved considerably in all other respects She has continued anticoagulant treatment as an out patient since and for a year has held her own but the clinical signs indicate that she still has moderate pulmonary hypertension

The case described by Castleman and Bland (1946) occurred in a woman of 35 following her third pregnancy she survived nine years of increasing obstruction and obliteration of the tertiary branches of the pulmonary artery the distal vessels remaining normal

The physical signs X ray and electrocardiographic appearances physiological findings course prognosis and detailed treatment of subacute thrombo embolic pulmonary hypertension are the same as for primary pulmonary hypertension (page 839) and will not be further considered here except to re emphasise the importance of prolonged rest and anti coagulant therapy the goal being a normal pulmonary vascular resistance It is not enough to prevent further embolism it may well be essential to keep the pulmonary blood pressure as low as possible for several months so that secondary proliferative changes and reactive pulmonary vaso constriction are discouraged Only when the resistance has fallen to normal should ordinary activities be resumed and pulmonary blood pressure lowering agents abandoned

Subacute obliterative pulmonary hypertension

The best examples of this condition are caused by periarteritis dissemi nated lupus and pulmonary schistosomiasis The first two have already been discussed to some extent in the section on cardiopathies of obscure origin and it is only necessary to add that both may cause obliterative pulmonary hypertension as a result of widespread arteritis involving the small vessels (Eskelund 1943) The clinical picture in this respect does not differ from any other kind of subacute pulmonary hypertension

Schistosomiasis has been recognised as a cause of pulmonary hyper tensive heart failure in Egypt for over twenty years (Azmy 1932) Either intestinal bilharziasis due to S Mansoni or urinary bilharziasis due to S hæmatobium may be responsible (Shaw and Ghareeb 1938) Ova from S Mansoni only reach the lungs when sufficient cirrhosis has developed to have resulted in anastomotic channels between the portal and systemic venous systems so that hepatosplenomegaly is invariably present in these cases ova from S hæmatobium can pass directly to the lungs The ova lodge in the arterioles, where they set up an acute obliterative necrotising arteriolitis, which is the cause of the pulmonary hypertension A specific angiomatoid lesion often develops in relation to capillary recanalisation of the occluded vessels (Shaw and Ghareeb 1938) Ova that escape through the wall of the arteriole cause the characteristic parenchymatous giant celled bilharzia tubercle (Sorour 1928) but these play no part in the syndrome under discussion Proximal to the sites of oval impaction the small arteries hypertrophy and develop marked intimal thickening—the usual reaction to pulmonary hypertension however caused

Clinically males are affected more often than females and the majority of patients are between 12 and 35 years of age Once pulmonary hyper tension has developed the clinical course and findings are like those of primary pulmonary hypertension (Bedford *et al* 1946) and death from congestive failure is likely within two years

A bedside diagnosis is usually possible as demonstrated by Kenawy (1950) It is based on (1) clinical features resembling those of

Hypoxic pulmonary hypertension

Pulmonary vasoconstriction which is not abolished by vagotomy or stellate ganglionectomy undoubtedly occurs in response to reduced alveolar oxygen tension both in animals (von Euler and Liljestrand 1946) and man (Motley *et al*, 1947) This response to oxygen lack is opposite to what occurs in the systemic circulation and has the advantage of deflecting the pulmonary blood flow from poorly ventilated zones (Liljestrand, 1948)

At first it seemed likely that this mechanism might be responsible for the pulmonary hypertension of anoxic cor pulmonale but it was soon discovered that the vasoconstrictive response seemed to occur only in acute experiments or clinical situations and was not maintained in the presence of chronic anoxia from advanced emphysema (Mounsey *et al* 1952) Nevertheless the reaction is clinically very important and explains why pulmonary hypertensive heart failure may be precipitated so easily by an attack of acute bronchitis in cases of chronic cor pulmonale and why oxygen therapy in such cases is so much more important than digitalis and elimination of sodium

REACTIVE PULMONARY HYPERTENSION

This group characteristically includes all those cases with a high or extreme pulmonary vascular resistance that has developed in response to passive or hyperkinetic pulmonary hypertension (Wood 1952) e g pulmonary hypertensive mitral stenosis (page 540) 'false Bernheim's syndrome (page 774) and the whole of the Eisenmenger group (page 397) but it may also include many cases in which pulmonary hypertension was caused initially by obstructive, thrombo embolic or obliterative vascular lesions and has been perpetuated by a similar reaction Whether or not hypoxic pulmonary hypertension is ever maintained long enough to be perpetuated in this way is uncertain but it is a possibility that should be borne in mind when attempting to synthesise the variable manifestations of cor pulmonale

The mechanism is not yet known for certain The belief that structural changes such as fibroelastic thickening of the intima of the small arteries and arterioles develop in response to passive or hyperkinetic pulmonary hypertension and gradually obliterate the pulmonary vascular bed and so cause secondary obliterative pulmonary hypertension is in the author's view untenable in the light of the known clinical and physiological data Evans (1951) went so far as to postulate a congenital deficiency of the media of the small pulmonary arteries in these cases and believed that fibro-elastic thickening was a protective reaction which finally obstructed the pulmonary circulation and caused obliterative pulmonary hypertension

But it has been repeatedly pointed out that reactive pulmonary hypertension is *not* a late manifestation of mitral stenosis left ventricular failure patent ductus, ventricular septal defect or atrial septal defect but if

occurs at all it develops early pari passu with the critical passive or potentially hyperkinetic pulmonary hypertension caused by the lesions mentioned (Wood 1952 1954) This behaviour categorically denies that a secondary obliterative process is responsible for the initial reaction although it no doubt increases the already raised resistance as the years go by

Again it is nearly always possible to lower the pulmonary vascular resistance in cases of reactive pulmonary hypertension by injecting acetyl choline aminophylline or priscoline into the pulmonary artery and this would not be expected in obliterative pulmonary hypertension

Finally whenever passive or hyperkinetic pulmonary hypertension is relieved by surgical correction of the responsible lesion the pulmonary vascular resistance falls which does not harmonise with the mechanistic hypothesis

For these reasons it is believed that reactive pulmonary hypertension is due to active vasoconstriction, and that anatomical changes in the small pulmonary blood vessels are secondary, but such a mechanism awaits proof There is good evidence that neither an elevated pulmonary venous pressure chronic interstitial oedema an increased pulmonary pulse pressure dilatation of the pulmonary artery or alteration of the alveolar or blood gas tensions is responsible for the reaction The tentative hypothesis that in certain individuals pulmonary vasoconstriction develops in response to pulmonary hypertension itself (Wood 1952) fits the known facts best, and harmonises with the current theory that chronic essential hypertension in the systemic circulation may be initiated by any other form of systemic hypertension and once developed may be self perpetuating (Smirk 1949) If the hypothesis is correct reactive pulmonary hypertension should develop also in a proportion of cases of obstructive or obliterative hypertension which should then be perpetuated in the same way long after the initial cause has subsided The behaviour of certain thrombo embolic cases does not deny this possibility

Clinically reactive pulmonary hypertension in cases of mitral valve disease left ventricular failure and the Eisenmenger group has already been discussed in detail and will not be further considered here

PRIMARY PULMONARY HYPERTENSION

There remains for discussion the enigma known as primary idiopathic or essential pulmonary hypertension

Incidence

In a consecutive clinical series of approximately 10 000 cases of cardio vascular disease of all types personally examined by the author since the second world war there were 17 instances of primary pulmonary hyper tension (0 17 per cent) These were all diagnosed clinically in the first

instance all but two were confirmed by cardiac catheterisation and the ten that died (which include the two not catheterised) were confirmed at necropsy So far no case in which the final clinical diagnosis was primary pulmonary hypertension has been disproved by subsequent necropsy This should be enough to emphasise the highly distinctive nature of the syndrome and to re affirm that it is a disease entity in its own right whatever the cause

In my series there were 14 females and 3 males In Brenner s exhaustive analysis of the literature up to 1935 he could only find 16 convincing cases of primary pulmonary vascular sclerosis as it was then called but he did not give their ages or sex From my own files of the literature however I have records of another 20 acceptable cases making 27 in all although many more have been reported These include the cases of Brenner (1935) 1 Seely (1938) 1 de Navasquez *et al* (1940) 2 of their 3 East (1940) 3 Barrett and Cole (1946) 1 Gold (1946) 1 Gilmour and Evans (1946) 1 Rosenbaum (1947) 2 Dresdale *et al* (1951) 3 and Soulie *et al* (1955) 5 Of the total there were 28 females and 9 males This female preponderance may well prove important

The ages of these thirty seven patients ranged between 4 and 68, the average being 31 Four were children or adolescents twenty two were young adults between the ages of 20 and 40 eight were between 40 and 50 and three were over 50 Primary pulmonary hypertension in infants has also been described (Wolman 1950)

Pathology

Since Brenner s careful description the majority of authors have con firmed the great variability of the lesions Considerable dilatation of the pulmonary artery is almost invariable Atherosclerosis is common in the major arteries particularly in the older patients and is regarded as a secondary change secondary thrombosis may occur It is in the small arteries and arterioles that the most significant lesions are found these include fibroelastic thickening of the intima (Barrett and Cole 1946) a d hypertrophy of the media (Brenner, 1935) but normal vessels are nearly always seen as well and in several cases all the small vessels have looked normal (de Navesquez *et al* 1940 East 1940) McKeown (1952) more over demonstrated that all the peripheral vascular lesions that have been reported as characteristic of pulmonary hypertension may be found in controls in the same age groups, which makes accurate interpretation very difficult

There are two other findings which must not be passed by Gilmour and Evans (1946) described hypoplasia of the media of many small vessel which they believed was congenital in origin and found that endarteritis fibrosa was closely related and presumably secondary to the defect In Gold s case (1946) there was also hypoplasia of the media and widespread secondary thromboses When old and new clots are a feature of the case

thrombo embolic obstructive hypertension with secondary obliterative changes is the more likely diagnosis

In my own cases the degree and extent of proliferative changes in the small arteries and arterioles was usually quite outside the range of what may be seen in controls but they could well have been secondary to the hypertension rather than its cause

Physiology

The high pulmonary vascular resistance imposes a heavy burden on the right ventricle which hypertrophies accordingly the right atrium gives maximum support and increases right ventricular diastolic stretch Despite these compensatory devices the cardiac output is low and on effort the right ventricle is readily overloaded (Howarth and Lowe 1953) so that the output may fall and result in syncope, whilst the reduced coronary flow may cause angina pectoris The arterial oxygen saturation remains normal until near the end and cyanosis is peripheral unless there happens to be a patent foramen ovale through which there may be a small reversed interatrial shunt

Physiological measurements were completed in 12 of my cases and were very similar to those reported by Dresdale *et al* (1951) *The pulmonary vascular resistance* averaged 15 units and ranged between 10 and 26 As Dresdale said this is about eight times the normal it is the same as is commonly found in fully developed reactive pulmonary hypertension in mitral stenosis and the Eisenmenger group

The pulmonary systolic blood pressure was well over 100 mm Hg (145 mm Hg) in only one instance in two cases it hovered round the 100 mark and in the rest it was only 65 to 90 mm Hg The diastolic pressure averaged 40 per cent of the systolic These unexpectedly low figures were attributed to right ventricular failure although at the time of catheterisation after treatment for congestive failure the right ventricular diastolic pressure was rarely much elevated Two of Dresdale s three cases also had pulmonary systolic pressures under 100 mm Hg

The cardiac output averaged 3 8 litres per minute in 11 adults and ranged between 2 6 and 4 5 at rest *The arterio venous oxygen difference* averaged 64 ml per litre the range being 56 to 80 Dresdale s figures were similar

The arterial oxygen saturation ranged between 88 and 95 5 per cent and averaged 92 per cent Each of Dresdale s cases was fully saturated

Clinical features

Symptoms include increasing effort intolerance due to fatigue, breathlessness angina pectoris or syncope Fatigue and breathlessness are forerunners of congestive heart failure Angina pectoris occurred of my cases and in two of 18 collected from the literature this incidence of 11 5 per cent syncope occurred in four of

and in four of 18 collected from the literature, i e in 23 per cent All my cases developed congestive failure, including those that are still alive

On examination the *physical signs* are highly characteristic and since they constitute the prototype of all kinds of pulmonary hypertension they are given here in full

1 Cyanosis when present is peripheral not central unless there is a reversed shunt through a patent foramen ovale which has been mentioned in necropsy reports in several instances The face may be highly coloured and bloated as in severe pulmonary valve stenosis but this is exceptional The hands are cold and blue as a rule unless hepatic failure causes vasodilatation and a palmar flush

2 The peripheral pulse is small

3 The rhythm is normal at first but towards the end paroxysmal or permanent atrial flutter or fibrillation is not uncommon in the more chronic cases

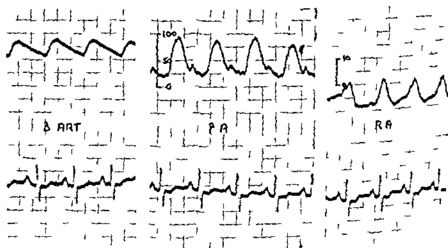


FIG 18 o.—Pressure pulse from the brachial artery pulmonary artery and right atrium in a case of primary pulmonary hypertension showing giant *a* waves in the right atrial tracing

4 The jugular venous pressure pulse reveals a giant *a* wave measuring 5 to 10 cm above *c* in three quarters of the cases (fig 18 o.) When there is advanced right ventricular failure the right atrium may also fail and the giant *a* may then disappear *v* becoming proportionately larger Functional tricuspid incompetence may also have this effect

5 Right atrial gallop rhythm and presystolic hepatic pulsation usually accompany the giant *a* wave

6 The left ventricle is impalpable but there is usually a powerful heave over the right ventricle between the left sternal border and mid clavicular

line Sometimes the right ventricle occupies the position of the apex beat Pulmonary artery pulsation was palpable in 60 per cent of my cases

7 There are five auscultatory signs right atrial gallop a tricuspid pan systolic murmur sometimes accompanied by a thrill when there is functional tricuspid incompetence (often heard well to the left since the dilated right ventricle occupies the apex beat) a sharp high pitched pulmonary ejection click over the dilated pulmonary artery a closely split second heart sound with sharp accentuation of the second or pulmonary element and a Graham Steell pulmonary incompetent diastolic murmur occasionally accompanied by a thrill in 40 per cent of cases An appreciable pulmonary ejection murmur is rare

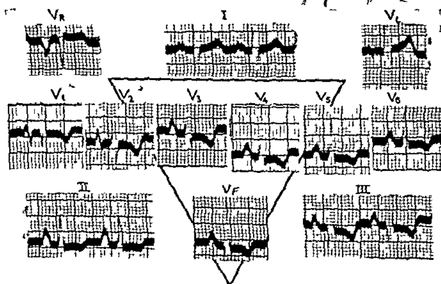


Fig 18 03—Electrocardiogram from a case of primary pulmonary hypertension showing a conspicuous P pulmonale and gross right ventricular preponderance

8 Signs of congestive heart failure are inevitable sooner or later

The *electrocardiogram* classically shows a conspicuous P pulmonale and gross right ventricular preponderance (fig 18 03)

X *rays* reveal a small aorta considerable *dilatation* of the pulmonary artery a variable degree of enlargement of the right ventricle and atrium an inconspicuous left ventricle and atrium and light peripheral vascular markings (fig 18 04)

Cardiac catheterisation reveals the physiological situation previously described If *acetylcholine* 1 mg is injected quickly into the pulmonary artery the pulmonary vascular resistance *falls* the pulmonary systolic and diastolic pressures fall the cardiac *output* rises (by 20 per cent in the case illustrated) the systemic blood pressure rises, and the heart rate

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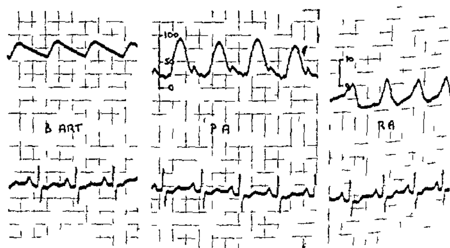


Fig 18 02—Pressure pulse from the brachial artery pulmonary artery and right atrium in a case of primary pulmonary hypertension showing giant *a* waves in the right atrial tracing

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5 Right atrial gallop rhythm and presystolic hepatic pulsation usually accompany the giant *a* wave

6 The left ventricle is impalpable but there is usually a powerful heave over the right ventricle between the left sternal border and mid clavicular

reflexly (fig 18 0,) The advantage of using acetylcholine in these studies is that in the dose used it is virtually inactivated by the time it reaches the systemic circulation and therefore has a selective action on the pulmonary vessels The effect is immediate begins with the first heart beat following the injection and proves conclusively that some degree of vasoconstriction whether physiological or pathological is present in these cases if anatomical obstruction of more than two thirds of the total cross section of the pulmonary vascular bed is in fact present, then the relatively healthy vessels are maintaining disadvantageous vasoconstrictor tone alternatively the high resistance is due at least in part to abnormal functional vaso constriction

Differential diagnosis

Clinically the diagnosis of severe pulmonary hypertension secondary to a high pulmonary vascular resistance is usually obvious the only question at issue being whether it is primary obstructive obliterative or reactive and at the bedside this may not be answered at all easily If the onset of symptoms follows pregnancy phlebothrombosis a surgical or dental operation or an accident thrombo embolic obstructive or secondarily obliterative pulmonary hypertension is more probable if indeed this is not the cause of all cases Disseminated lupus periarteritis and schistosomiasis should be considered and tell tale clues searched for In primary pul monary hypertension all laboratory tests are negative

Reactive pulmonary hypertension due to mitral stenosis is probable if there is a history of rheumatic fever or chorea if the mitral first sound is sharp if a faint opening snap can be heard or recorded phonocardio graphically if slight dilatation of the left atrium can be demonstrated radiologically or if the electrocardiogram shows a P mitrale No difficulty of course arises if the classical signs of mitral stenosis are not masked by the large right ventricle In one of the author s cases the only clinical evidence of mitral stenosis was slight calcification of the mitral valve but this was considered conclusive and successful mitral valvotomy was carried out

Reactive pulmonary hypertension associated with patent ductus ven tricular septal defect or atrial septal detect is at once suggested if there is any direct or indirect evidence of central cyanosis or reduced arterial oxygen saturation at rest or on effort whether generalised as in atrial septal defect and ventricular septal defect or chiefly confined to the lower half of the body as in patent ductus In adults the history alone usually proves the congenital nature of the disease but in acyanotic children the differential diagnosis may not be ea y at the bedside Giant *a* waves however deny an alternative route for blood ejected from the right ventricle and therefore exclude patent ductus and ventricular septal

A loud pulmonary ejection murmur is much in favour of one Eisenmenger group in which the pulmonary blood flow aver

that in primary pulmonary hypertension A pure single second heart sound favours Eisenmenger s complex proper (with ventricular septal defect) and a relatively widely split second sound favours pulmonary hypertension with atrial septal defect Any clinical electrocardiographic or radiological evidence proclaiming a state of balanced ventricular work at once denies primary pulmonary hypertension and is strongly in favour of patent ductus or ventricular septal defect with reactive pulmonary hypertension

When in doubt the correct diagnosis may be established in most cases by means of cardiac catheterisation with or without the help of Evans blue or other dye Angiocardiography may also prove the presence and site of a reversed shunt The simplest out patient test, however, is to see whether or not the arterial oxygen saturation falls on effort this may be detected by means of an ear oximeter in cases of Eisenmenger s complex and pulmonary hypertension with reversed interatrial shunt and by means of femoral artery samples in cases of pulmonary hypertension with reversed aorto pulmonary shunt through a patent ductus

Course

The average duration of life from the onset of symptoms in 20 fatal cases was 3 2 years the range one month to 10 years It is not without significance that so far no early case has yet been diagnosed It was at one time suspected that mass radiography might reveal an occasional early case but this has not proved to be so of 10 patients discovered to have unexplained dilatation of the pulmonary arc for example but who were symptom free and without abnormal physical signs cardiac catheterisation revealed normal physiology This persistent failure strongly suggests that the disease is subacute rather than chronic and so it would be if it were initially thrombo embolic in origin

Treatment

No effective treatment has yet been devised for primary pulmonary hypertension Dresdale (1951) suggested priscoline but it has proved valueless in my cases although when injected directly into the pulmonary artery in a dose of 10 mg it undoubtedly lowers the pulmonary vascular resistance as does acetylcholine and aminophylline I have tried oral priscol 25 to 50 mg t d s aminophylline 0 2 G t d s etophylate 0 5 G t d s and hexamethonium bromide 500 to 750 mg t d s before meals all without the slightest effect I have also tried permanent anticoagulant therapy with dindevan on the chance that recurrent thrombo-emboli m was responsible but without avail Cortisone merely aggravated heart failure as a result of sodium retention and prednisone proved little less harmful in one case in which it was tried for several months In desperation on one occasion Blalock s operation of subclavian pulmonary artery anastomosis was attempted in the hope of providing a safety valve for the

pulmonary circulation but the patient died of ventricular fibrillation on the operating table

At the present time and in the light of what is known or suspected, there is a chance that a combination of strict bed rest or total inactivity priscol theophylline and ansolysen and permanent anticoagulant therapy may favourably influence a small number of cases which fulfil the clinical criteria for a diagnosis of primary pulmonary hypertension When heart failure is present it should be treated in the usual way

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CHAPTER XIX

COR PULMONALE

Definition

The term cor pulmonale is best reserved to identify a specific cardiovascular disorder secondary to disease of the lung parenchyma although classically chronic it may be subacute or even acute

Incidence

It is difficult to estimate the prevalence of cor pulmonale for several reasons (1) the disease is rarely so labelled until there is congestive heart failure (2) its distribution is patchy apparently being more common in large industrial cities than elsewhere (3) in view of the frequency with which its clinical manifestations are precipitated by acute bronchitis or bronchopneumonia most cases are admitted to general hospitals rather than cardiovascular clinics and the recognition of cor pulmonale often depends a great deal on the interest of the physician concerned In the Registrar General s review for 1953 the disease is not listed at all as such but there were 30 392 deaths from bronchitis (6 per cent of the total mortality for England and Wales for that year) and 15 661 deaths from bronchopneumonia During the same year there were 61 751 deaths from ischæmic heart disease (12 per cent) 20 423 from hypertensive heart disease (4 per cent) and 8 837 from chronic rheumatic heart disease (1 8 per cent) Now in a general hospital in Sheffield according to Flint (1954) cor pulmonale accounted for 25 per cent of 300 cases of *congestive heart failure* ischæmic heart disease for 22 per cent hypertensive heart disease for 21 per cent and rheumatic heart disease for 23 per cent At the other extreme there is my own small series of only 45 proved cases of cor pulmonale amongst a consecutive series of about 10 000 clinical cases of cardiovascular disease of all types seen at specialised clinics and in private practice Realistic figures are therefore impossible to compile at the present time A reasonable conservative guess for the frequency of chronic cor pulmonale might be 5 to 10 per cent of all cases of organic heart disease

Cor pulmonale is at least five times more common in men than in women and about 75 per cent of the patients are over 50 years old (Spain and Handler 1946)

Pathogenesis

There are only two fundamental factors concerned with the development of cor pulmonale hypoxia and obliterative changes in the pulmonary

circulation The degree to which each contributes determines the clinical features and course of the disease Carbon dioxide retention may modify the symptoms but not the essential cardiovascular hæmodynamics

Hypoxia is commonly due to emphysema and is much aggravated by attacks of bronchitis bronchopneumonia and bronchial asthma which *themselves are usually responsible for the emphysema The chief difficulty* is ventilatory an insufficient number of alveoli are filled with fresh air at each breath Blood that perfuses unventilated alveoli cannot absorb oxygen or eliminate carbon dioxide The arterial oxygen tension *therefore* falls and the carbon dioxide tension rises in turn this results in reduced arterial oxygen saturation (McMichael and Sharpey Schafer 1944) and increased arterial carbon dioxide content (Taquini *et al* 1947)

Hypoxia however may also occur as a result of difficulty in oxygen *perfusion* across the alveolar capillary interface when the boundary zone is thickened in any way Carbon dioxide, being twenty five times more soluble in water than oxygen and therefore equally more diffusable, rarely experiences this difficulty so that in these cases hypoxia *is not associated* with carbon dioxide retention (Baldwin Cournand and Richards 1949) Arnott (1955) gives the chief causes of difficulty in oxygen diffusion as diffuse interstitial pulmonary fibrosis sarcoidosis silicosis inhalation of beryllium scleroderma radiation fibrosis and diffuse carcinomatosis

Hypoxia however produced results in central cyanosis vasodilatation an increased cardiac output (McMichael and Sharpey Schafer 1944) and polycythæmia *It is the hypoxia that is responsible for the hyperkinetic character of the circulation in cor pulmonale* During acute episodes of bronchitis bronchopneumonia or bronchial asthma the alveolar oxygen tension falls as a result of the increased ventilatory difficulty This causes *transient pulmonary vasoconstriction (Motley et al 1947) further reduc*tion in arterial oxygen saturation and a secondary rise of cardiac output in a group of cases described by Donald (1953) the mean pulmonary artery pressure rose from an average of 25 mm Hg to 50 *mm Hg during* such episodes This puts a heavy burden on the right ventricle which is asked to increase its stroke volume against an increased resistance and congestive failure is common

Obliteration of a sufficient cross section of the pulmonary vascular bed to raise the pulmonary blood pressure at rest is unusual in both emphysema and interstitial pulmonary fibrosis but there is frequently sufficient obstruction to cause obliterative pulmonary hypertension when *the cardiac output is raised in response to effort or hypoxia* (Bloomfield *et al* 1946 Harvey *et al* 1951) In my own series of 45 cases of well established cor pulmonale the pulmonary vascular resistance was between 6 and 10 units in 20 per cent and over 10 units (extreme) *in* a further 20 per cent but the arterial oxygen saturation in these two groups was no lower than in the 60 per cent of cases that had normal or only slightly raised resistances averaging 85 per cent at rest when free from infection and bronchospasm

irrespective of the resistance This lack of correlation is not surprising for the lower the arterial oxygen saturation the more the perfusion of un ventilated alveoli and this means non obliterated capillaries in the non functioning zones which would not encourage pulmonary hypertension Admittedly the pulmonary blood pressure may be higher in the more anoxic patients but this may be explained by the higher cardiac output

Whether or not the 20 per cent of cases with pulmonary vascular resistances *in the extreme range have reactive* vasoconstriction or merely advanced obliterative pulmonary hypertension remains to be seen Such a group would be expected if there is anything in the hypothesis propounded in the last chapter There is no doubt that secondary atherosclerosis thrombosis medial hypertrophy and fibroelastic intimal thickening may develop as a result of the long standing pulmonary hypertension and add their own obstructive or obliterative burden

Clinical features

The patient is usually *a middle aged or elderly man* He *commonly* gives a history of bronchial asthma or of recurrent winter bronchitis for many years with increasing breathlessness over the last year or two, and may have sought advice because of recent swelling of the legs Cross examination yields little further information he may have had attacks of tightness in the chest associated with breathlessness but not paroxysmal cardiac dyspnœa he may have had substernal discomfort, but not true angina he may prefer to be propped up a little at night but usually raises no objection to lying flat Headache attributed to a raised C S F pressure was noted in 55 per cent of Flint s series *Dyspnœa is attributed to oxygen lack carbon dioxide* retention (until the respiratory centre becomes insensitive) decreased pH and mechanically to the extra effort required to inflate and deflate the lungs (Christie, 1944)

In a minority of cases there may be historical clues pointing to the nature of the underlying lung disease e g symptoms of bronchiectasis established pulmonary tuberculosis pneumonectomy or thoracoplasty, Pott s disease of the spine or bronchopneumonia in the last London fog Cases with oxygen diffusion difficulty may give a history of severe and increasing *breathlessness on effort for which they have received* scant sympathy or they may mention occupational hazards of silicosis asbestosis or beryllium poisoning cutaneous or other lesions suggesting *sarcoid or scleroderma* deep X ray therapy for carcinoma of the lung or just a single attack of virus pneumonia Occasionally the onset of congestive heart failure is heralded by no previous symptoms whatsoever

Physical signs

Emphysema is usually obvious the chest is distended and moves little with respiration cardiac dullness is absent and the percussion note is generally tympanitic the breath sounds are faint Wheezing and

denote bronchospasm or active bronchitis and the latter may also cause widespread coarse rales and mucopurulent sputum Central cyanosis may be gross or scarcely detectable It may be recognised in warm situations as in the conjunctivæ and inner sides of the lips where it is unlikely to be confused with peripheral cyanosis The hands are warm and the forearm veins distended capillary pulsation digital throbbing a modified water hammer pulse and increased pulse pressure may often be demonstrated (fig 19 01) Clubbing may occur but is unusual and pulmonary osteo

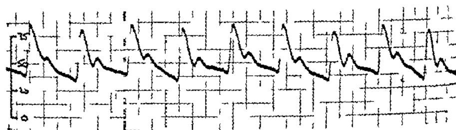


Fig 19 01 – Brachial arteriogram showing a typical waterhammer pulse in a case of anoxic cor pulmonale

arthropathy is more so Slight elevation of the jugular venous pressure and tachycardia may confirm the impression that the cardiac output is raised Papillœdema sometimes occurs and may be attributed to a raised C S F pressure associated with a greatly increased cerebral blood flow secondary to carbon dioxide retention (Simpson 1948)

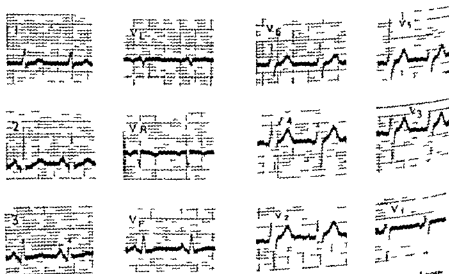


Fig 19 02—Electrocardiogram in a case of emphysema showing a vertical electrical position and clockwise rotation (viewed from below)

The heart itself is apt to be camouflaged by over expanded lung the apex beat is impalpable the left cardiac border impossible to locate by percussion the heart sounds difficult to hear and the second sound at the base often inaudible there are no murmurs but right sided summation gallop may be heard or felt just to the left of the sternum in the fourth intercostal space or in the epigastrium

When there is congestive heart failure the venous pressure is higher the liver distended and tender and œdema usually considerable the signs of a hyperkinetic circulatory state may remain or disappear gallop rhythm becomes diastolic in time and there may be functional tricuspid incompetence When the pulmonary vascular resistance is high in cor pulmonale the clinical findings are quite different, central cyanosis is still present but there may be peripheral cyanosis as well, the hands are cold and blue the forearm veins constricted, and there is no evidence of a hyperkinetic circulation, there may be a giant *a* wave in the jugular pulse and gallop rhythm is presystolic

In severe cases vasomotor collapse is apt to occur when some superimposed broncho pulmonary infection lowers the arterial oxygen saturation relatively suddenly the blood pressure drops the pulse becomes small and thready the cardiac output low and the skin cold and clammy the outlook is then very grave

The electrocardiogram Emphysema alone does not materially affect the electrocardiogram although it may cause clockwise rotation about the antero posterior and longitudinal axes (viewed from the front and below) Thus there may be right axis deviation in standard leads an RS pattern in lead V_L a QR pattern in lead V_F and an RS pattern from V_1 as far as V_5 or even V_6 (fig 19 02) When the heart is exceptionally vertical V_R and V_L may be indistinguishable or backward tilting of the apex may cause V_L to resemble an œsophageal lead from the back of the heart

In 100 cases of chronic cor pulmonale analysed by the author (Wood 1947) the following electrocardiographic appearances were found *in standard leads* (fig 19 03a to e)

Pulmonary P wave	85
Right axis deviation—	
with T3 (and often T2) inverted (a)	20
with T upright in all leads (b)	30
Prominent S wave in all leads (c)	9
Tendency to right axis deviation (d)	11
Normal axis of QRS (e)	26
Right bundle branch block	4
Low voltage	40

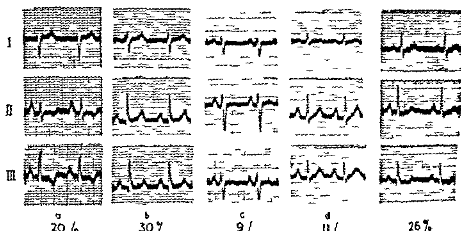


Fig 19 03—Standard lead electrocardiographic findings in 100 cases of cor pulmonale
(a) Right axis deviation with inversion of T3 (and often T2)
(b) Right axis deviation with upright T waves
(c) Dominant S wave in all standard leads
(d) Tendency to right axis deviation
(e) Normal QRS axis
The pulmonary P wave is seen in all

Multiple chest leads revealed the following (fig 19 04a to e)

Normal QRS deflections in the majority (a and b)	
Inversion of T from V_1–V_3 (c)	13
Dominant R wave in V_1 with conspicuous S in V_5 (d)	16
Dominant S wave from V_1–V_5 (e)	16

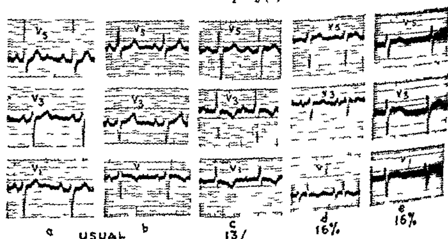


Fig 19 04—Chest lead findings in cor pulmonale
(a) (b) Normal chest leads
(c) Inversion of T from V_1 to V_3
(d) *Dominant* R wave in V_1 with *conspicuous* S in V_5
(e) Dominant S wave from V_1 to V_5





(a) (b)

Fig 19 05 (a) (b)—Skiagrams of two advanced cases of cor pulmonale showing dilatation of the pulmonary artery and of the left and right branches





(a) (b)

Fig 19 06 (a)—Right anterior oblique position showing the increased density and diameter of the pulmonary artery at its bifurcation
(b) Left anterior oblique position showing the left pulmonary artery forming an arc almost as dense and as large as the aortic arch

Unipolar limb leads nearly always showed a vertical electrical position

The pulmonary P wave is probably the earliest sign of cardiovascular disturbance resulting from emphysema or at least competes in this respect with elevation of the right ventricular pressure and slight reduction of the arterial oxygen saturation it may develop several years before the onset of heart failure

As would be expected the degree of right ventricular preponderance is proportional to the pulmonary artery pressure and pulmonary vascular resistance (Johnson *et al* 1950)

Fluoroscopy Prominence of the main branches of the pulmonary artery at the hila with or without dilatation of the main pulmonary arc is seen in over 50 per cent of cases of severe emphysema (Parkinson and Hoyle 1937) but the changes are rarely conspicuous until cor pulmonale is well advanced (fig 19 05 and 19 06) Associated hypertrophy of the right ventricle is less easily demonstrated

Pulsation of the pulmonary artery and its main branches may be seen sometimes but does not compare with that in atrial septal defect and as a rule is absent Peripheral vascular markings are relatively unimpressive Enlargement of the right atrium is rare in the absence of failure The left atrium is flat and a prominence on the left border of the heart between the pulmonary and left ventricular arcs is never seen Owing to the raised cardiac output and the average age of these patients the aortic knuckle is usually well seen and may be unduly prominent



Fig 19 07—Skiagram of a case of advanced anoxic cor pulmonale due to emphysema with a normal pulmonary vascular resistance showing a cardiovascular contour having no resemblance to the traditional descriptions

The changes described are not as frequent as originally supposed and are much more typical of the 40 per cent of cases that have a high pulmonary vascular resistance than of the 60 per cent that have not (fig 19 07) It is this unfamiliarity with the nondescript appearance of the cardiac shadow in many cases of advanced cor pulmonale with a raised cardiac output and normal resistance that has so often led to the diagnosis being overlooked Indeed when there is moderate coincident essential hypertension or ischæmic heart disease cases may actually present with left ventricular failure as in any other hyperkinetic circulatory state when the left ventricle carries the heavier load or is weakened by intrinsic

disease such cases are erroneously diagnosed as hypertensive or ischæmic heart failure

Then there may be evidence of emphysema widening of the rib spaces elevation of the ribs and clavicle depression of the diaphragm and increased translucency of the lung parenchyma However it is notoriously difficult to diagnose the degree of emphysema from the radiological appearances and in any case emphysema is not cor pulmonale

Finally X rays may reveal the nature of any underlying disease of the lungs that may be causing or behaving like emphysema such as bronchiectasis or honeycomb lung (fig 19 11) any of the diseases listed earlier that may cause interstitial fibrosis (fig 19 09) diffuse carcinomatosis (fig 19 10) or perhaps a surprise such as a massive bulla aneurysm or thrombosis of a main pulmonary artery (fig 18 01) As Flint (1954) pointed out pleural effusion is very uncommon in cor pulmonale owing to the frequency of obliterative pleurisy

Special investigations

The diagnosis of emphysema and its degree may be established by demonstrating static changes in the subdivisions of the lung volume namely a reduced vital capacity greatly increased residual volume or dead space diminished inspiratory capacity and a normal or increased total lung volume Typical findings were published by Whitfield *et al* (1951) as follows (for men)

	Normal controls (litres)	*Moderate emphysema (litres)*	*Severe emphysema (litres)*
Vital capacity	4 00	3 31	2 22
Residual volume	1 75	2 86	3 51
Expiratory reserve	1 27	1 05	0 70
Inspiratory capacity	2 73	2 26	1 52
Total lung volume	5 74	6 17	5 74

All workers in the field of emphysema however have found poor correlation between the degree of these changes and the grade of effort intolerance They are anatomical measurements and give little direct information about pulmonary function (Baldwin *et al* 1949)

The *maximum breathing capacity* is much reduced in emphysema and of course even more so when there is bronchospasm Over a 15 second test period of maximum respiratory effort only 20 to 30 litres per minute may be ventilated instead of the normal 75 to 100 litres per minute These low figures are due to mechanical difficulty in inflating and deflating inelastic emphysematous lungs and the reduced number of functioning alveoli It should be remembered that the maximum breathing capacity is an artificial test over a very short period of time and that normal subjects become dyspnœic when ventilating more than half their test figure

The *resting ventilation* (normally around 6 to 7 litres per minute) varies considerably according to the state of the blood gases the arterial pH and the sensitivity of the respiratory centre When the arterial pCO_2 and carbon dioxide content are high the respiratory centre is usually insensitive and respiration may be depressed in the presence of considerable anoxia Resting ventilation is more likely to be increased in emphysema when CO_2 retention is minimal and anoxia slight Much of the air inhaled is wasted in the increased dead space and unperfused alveoli or by over ventilation of relatively normal alveoli It follows that for each 100 ml of oxygen consumed more than the normal 2 5 litres of air must be breathed Thus the *ventilation equivalent for oxygen*, as this relationship is called is increased

Ventilation on effort is limited by mechanical respiratory difficulty It is usually expressed as a percentage of the maximum breathing capacity (Cournand and Richards, 1941) Patients with emphysema tend to develop very high ratios and complain less when the figure is over 50 per cent than patients with other respiratory diseases (Baldwin *et al* 1949)

Mixing efficiency is impaired in emphysema (Meneely and Kaltreider, 1941) If an inert gas like helium is inhaled it should reach all parts of the lung quickly and uniformly and the curve of its dilution should be rapid and uniform until mixing is complete In emphysema complete mixing is delayed for it takes longer for helium to reach the unventilated alveoli

The volume of the *poorly ventilated space* in emphysema can also be measured by the helium method and increases with the degree of emphysema

Analysis of the blood gases is the most important single measurement of the degree of emphysema Baldwin *et al* (1949) recognised four grades of severity in mild cases the arterial oxygen saturation was over 92 per cent at rest and did not fall on effort in moderate cases it was over 92 per cent at rest but fell on effort in grade 3 there was carbon dioxide retention in addition to a reduced arterial oxygen saturation at rest and in grade 4 there was heart failure in addition

Cor pulmonale only occurs in the two severe grades of emphysema and the average *arterial oxygen saturation* in my own cases was 85 per cent at rest This explains why central cyanosis is so often borderline The *arterial carbon dioxide content*, normally 44 to 53 ml per cent ranged between 62 and 71 vols per cent in a group of cases with heart failure studied by Platts and Whitaker (1954) More sensitive than measurement of the arterial oxygen content is that of the partial pressure of oxygen in arterial blood for this determines the quantity of oxygen that must combine with hæmoglobin The normal *arterial* pO_2 is about 100 mm Hg This may fall to as low as 62 while the *arterial oxygen* has only dropped to 90 per cent as the familiar oxyhæmoglobin dissociation curve shows (fig 19 08) Something is gained also by measuring the *arterial* pCO_2, for although a 5 per cent increase of CO tension results in approximately

a 5 per cent ri e of carbon dioxide content pCO is normally fixed close to 40 mm Hg so that quite small alterations are significant whereas the normal range of carbon dioxide content varies through 10 vols per cent from 44 to 53

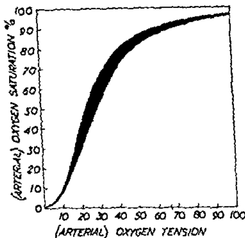


Fig 19 08—Composite oxyhaemoglobin dissociation curve (after Barcroft)

Again the CO_2 content of arterial blood is more helpful than the CO_2 *content of venous blood* the normal range for the latter varying between 53 and as much as 75 vols per cent

The plasma pH normally 7 41 is usually lowered in severe emphysema with cor pulmonale and ranged between 7 29 and 7 39 in the group of cases studied by Taquini *et al* (1947)

Finally estimation of the *alveolar capillary or alveolar arterial oxygen tension gradient* may give valuable information concerning oxygen diffusion across ventilated alveolar capillary membranes or the degree of perfusion of unventilated alveoli (venous admixture) High alveolar capillary oxygen tension gradients are characteristic of diffuse interstitial fibrosis (Donald *et al* 1952)

The pulmonary blood pressure and cardiac output may be measured by means of cardiac catheterisation Circulatory changes are unlikely to be present however unless the arterial oxygen saturation is below 92 per cent at rest and the arterial carbon dioxide content above 53 vols per cent When the pulmonary vascular resistance is normal or under 5 *units* the cardiac output is then raised but rarely above 10 litres per minute (McMichael and Sharpey Schafer 1944) When the resistance is high however the output is usually normal or even low Thus when both types are analysed together the net result is usually a high normal output around 6 litres per minute at rest

When pressures are normal at rest they may yet rise smartly on effort (Riley *et al* 1948)

Diagnosis

The usual clinical problem is to decide whether the cardiovascular system is involved in a known case of emphysema this is not at all difficult for it is simply a matter of deciding whether the arterial oxygen tension and saturation are reduced and whether or not the pulmonary blood pressure is raised If central cyanosis cannot be recognised the arterial oxygen saturation is not likely to be below 85 per cent If the oxygen

tension is down there should be good evidence of peripheral vasodilatation and a hyperkinetic circulatory state The ocular fundi may suggest carbon dioxide retention Signs of pulmonary hypertension should not escape notice If there is heart failure or simply œdema a diagnosis of cor pulmonale can usually be made with confidence under the clinical circumstances If there is any doubt blood gas analysis should resolve it

Difficulty may arise in distinguishing cor pulmonale from other cardiopathies and especially in unravelling a mixed etiology Other hyperkinetic circulatory states may have to be excluded particularly cirrhosis of the liver in emphysematous alcoholics but also thyrotoxicosis secondary carcinomatosis of the liver and Paget s disease of bone in emphysematous subjects The commonest mixed etiology is the association of emphysema and hypertension Although the differences between hypertensive heart failure and cor pulmonale are many it should be remembered that both may occur at the same time

In the stage of low blood pressure and reduced cardiac output clinical diagnosis may be more difficult Toxic vasomotor collapse from bronchopneumonia may cause confusion mitral stenosis Pick s disease mediastinal tumour the Eisenmenger group other forms of severe pulmonary hypertension and many other conditions may have to be considered The correct diagnosis can usually be made after full investigation but the first clinical impression can be misleading

Complications

Pulmonary hypertension a raised cardiac output the effects of a high C S F pressure polycythæmia pulmonary osteoarthropathy insensitivity of the respiratory centre carbon dioxide narcosis and a number of other features that might be considered as complications have all been treated as part of the disease itself Similarly the absence of angina pectoris rhythm changes pleural effusion phlebothrombosis have also been referred to *Congestive heart failure* however requires further comment

It has already been explained that heart failure may result from overwork (pulmonary hypertension and raised cardiac output) under hypoxic conditions According to Boniface and Brown (1953) a high carbon dioxide tension also depresses myocardial function There is however another important aspect of these cases that has been a source of much confusion—the effect on the circulation of a diminished renal plasma flow and diminished glomerular filtation This renal factor may come into play when the cardiac output is raised or well within the normal range (Lewis *et al* 1952) and causes sodium retention an increased blood volume (which masks polycythæmia) a rise of venous pressure and œdema when the heart is not overloaded On several occasions patients in this physiological state referred to the clinic because of heart failure have responded to physiological tests such as tipping and the Valsalva manœuvre like normal controls What constitutes heart failure proper and what does

not is largely a matter of definition but from the prognostic point of view the outlook is better in these cases than when the heart is overloaded

Prognosis

The diagnosis of chronic anoxic cor pulmonale usually carries with it a grave prognosis few cases surviving two years, but such diagnoses are rarely made before the onset of failure With the newer methods of investigation circulatory involvement should be recognised much earlier, perhaps by five years and appropriate treatment might then prolong life

Treatment

Vigorous preventive and symptomatic treatment of bronchitis and asthma may delay the development of serious emphysema indefinitely Half hearted measures must be condemned when the ultimate fate of these patients is realised

By the time the cardiovascular system is involved emphysema is usually far advanced A partly reversible state may be encountered however when acute bronchitis bronchopneumonia or an asthmatic bout is superimposed on chronic changes of only moderate degree In such cases infection should be treated promptly with penicillin or other forms of chemotherapy and bronchial spasm relieved by a dust free atmosphere and antispasmodics

Although details of such treatment cannot be considered in a work of this kind one or two observations are necessary Morphine is frequently lethal owing to its depressing effect on respiration pethidine may quieten a restless patient just as well is a good antispasmodic and does not depress respiration Subcutaneous adrenaline is still the most effective way of reliev ing bronchial spasm in an emergency newer remedies such as the anti histamine drugs may be given in addition but not as a substitute Isopropyl nor adrenaline which may be administered in sublingual tablets in doses of 20 to 40 mg is a useful preparation Antispasmodics that improve the cardiac output or coronary circulation such as aminophylline may be chosen in preference to those that do not An oral dose of 0 1 to 0 2 G t d s is usually insufficient and since repeated intravenous injections are impracticable and the intramuscular route too painful the only efficient way of giving aminophylline is by suppository 0 4 to 0 5 G twice daily Etophylate 0 5 G t d s or choline theophyllinate 0 5 G t d s however may be given by mouth as a substitute and etophylate is painle s intra muscularly

Whether the case is complicated by infection and bronchial spasm or not it is vitally important that the patient should be nursed in an oxygen tent The effect of improving the arterial oxygen saturation is often dra matic it prevents fatal vasomotor collapse reduces the cardiac output and may lower the pulmonary blood pressure The fear of carbon dioxide narcosis is no excuse for withholding the one remedy these patients need above all others It is true that some 10 per cent of patients with cor

pulmonale have developed such insensitive respiratory centres that they no longer respond to carbon dioxide but only to oxygen lack When oxygen is provided the increased arterial oxygen tension deprives the respiratory centre of its stimulus and respiration becomes depressed The arterial carbon dioxide tension may then rise very high indeed and the patient may become drowsy and finally lapse into coma (Davies and MacKinnon 1949) presumably with a high C S F pressure and cerebral œdema It is also true that oxygen is still given intermittently, but the fact remains that it is not given with sufficient enthusiasm nowadays, and patients are not recovering as quickly as they should in consequence As implied above 90 per cent of cases do not develop carbon dioxide narcosis when treated in an oxygen tent without any special precautions Moreover it has now been shown that the insensitivity of the respiratory centre is partly due to oxygen lack itself and may recover when oxygen is supplied (Westlake Simpson and Kaye 1955) Respiratory stimulants may also be given if drowsiness develops or an artificial respirator may be used Aminophylline may help and nikethamide may be given repeatedly in emergency Since aspirin may cause hyperventilation with secondary alkalosis by its direct action on the respiratory centre it has been tried recently in the cases under discussion (Wegria 1955) but since it also increases oxygen consumption by about 20 per cent (Tenney and Miller 1955) it is far from ideal

Mersalyl and a low sodium diet should be used with caution However McMichael and Sharpey Schafer (1947) have shown that in most cases with raised cardiac outputs the venous pressure is already at an optimum level and that lowering it by any means may *reduce* the output and harm the patient In a minority however the heart is overloaded and then responds to such treatment in the usual way Although clinically it may not always be easy to judge the physiological state of the circulation warm extremities and a full bounding pulse theoretically contraindicate all venous pressure lowering agents whereas cold extremities a small pulse and low blood pressure demand them (when the venous pressure is raised) When œdema is considerable and the jugular venous pressure over 7 cm above the sternal angle mersalyl and a low sodium diet should be tried Practical experience has proved their value and no harmful effects have been observed part of their usefulness is in removing what is virtually renal œdema

Venesection should certainly be avoided not only because its venous pressure lowering effect is too drastic and may be dangerous if ill judged but because correcting physiological polycythæmia results in a further increase of cardiac output a rise in pulmonary artery pressure and a fall in arterial oxygen saturation (Lewis *et al* 1952)

Digitalis or strophanthin may be used without fear if the heart is thought to be overloaded if in fact the output is raised and at its physiological maximum no harm will result from therapeutic doses

If, after relief of bronchial spasm and infection, the arterial oxygen saturation is still below 80 per cent when the patient is out of the tent antithyroid drugs should be seriously considered as a means of reducing the oxygen requirement (page 312)

SPECIAL FORMS OF COR PULMONALE

Diffuse interstitial pulmonary fibrosis

In 1944 Hamman and Rich described a hitherto unknown type of parenchymatous disease of the lungs of uncertain etiology characterised by alveoli lined with cuboidal cells and separated from one another by marked proliferation of the interstitial connective tissue In this condition the physical barrier between alveolar air and capillary blood is considerable and efficient oxygen diffusion difficult Carbon dioxide being 25 times more soluble in water than oxygen has little difficulty in crossing the barrier This results in reduced arterial oxygen tension and saturation without carbon dioxide retention indeed hyperventilation due to anoxia may result in reduction of the arterial pCO_2 and carbon dioxide content The respiratory centre remains highly sensitive in this condition and responds vigorously to any rise in CO tension

The subdivisions of the lung volume maximum breathing capacity, mixing efficiency and poorly ventilated space may be altered very little though the increased rigidity of the fibrotic lungs may add to the work of respiration the inspiratory reserve capacity may be reduced and the intrapleural pressure swings greater than normal

Clinically these patients complain of severe dyspnœa at a time when little abnormal may be detected and on this account may receive scant sympathy an erroneous diagnosis of respiratory neurosis being made for in the early stages the X ray appearances of the lungs may be normal But the reduced arterial oxygen tension leads to early peripheral vasodilatation and the warm hands, throbbing digital vessel and distended forearm veins should not escape notice On effort the arterial oxygen saturation which may be over 90 per cent at rest drops sharply and central cyanosis may then be detected clinically

The diffusion difficulty may be demonstrated by measuring the alveolar arterial oxygen tension gradient which is much increased above the normal of 5 to 10 mm Hg serious venous admixture is excluded by relatively normal ventilatory function tests

As the disease advances the circulation becomes more hyperkinetic and cor pulmonale with heart failure develops sooner or later as in the case described by Sloper and Williams (1955) Pulmonary hypertension has not been a feature of my own three cases but is said to develop sooner or later in most (Arnott 1955) Radiological evidence of the diffuse fibrotic change also becomes apparent as a fine reticular or ground glass appearance.

The prognosis and treatment are similar to emphysematous

pulmonale except that antispasmodics are not required and there is no danger of carbon dioxide narcosis

Other types of interstitial fibrosis

A very similar physiological situation may arise from any other disease that thickens the barrier between the alveoli and the capillaries of the lung Donald (1953) lists the following causes of serious diffuse interstitial fibrosis beryllium granuloma asbestosis scleroderma sarcoidosis reticuloses and interstitial pneumonitis', and Arnott (1955) adds radiation fibrosis silicosis and diffuse carcinomatosis

Although the nature of the etiological agent is obviously important and every effort should be made to identify it the development and course of cor pulmonale in each type follows the same familiar lines How often a serious diffusion difficulty accompanies chronic interstitial œdema in mitral stenosis and left ventricular failure is at present uncertain In figure 19 09 the radiological appearances in a case of interstitial fibrosis are illustrated This woman who was very breathless on exertion also had signs of mild mitral stenosis but cardiac catheterisation revealed a left atrial pressure under 5 mm Hg a mean pulmonary artery pressure of only 13 mm Hg, a cardiac output of 4 1 litres per minute and an arterial oxygen saturation of 86 5 per cent The radiological appearances are not unlike those of chronic interstitial œdema but in view of the findings independent interstitial fibrosis seemed inescapable

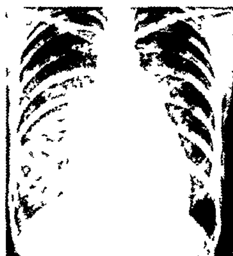


Fig 19 09—Diffuse interstitial pulmonary fibrosis in a case of mild mitral stenosis

Cor pulmonale from pneumoconiosis

Although many papers have described the frequency and course of cor pulmonale in pneumoconiosis (e g Coggin *et al* 1938 Thomas 1948) it is not yet clear whether emphysema interstitial fibrosis or obliterative pulmonary hypertension is chiefly responsible or whether a variable combination of all three factors are to blame Further detailed physiological studies are awaited with interest

Diffuse carcinomatosis

In previous classifications diffuse carcinomatosis has usually been regarded as a special form of subacute obstructive ' cor pulmonale when the term cor pulmonale included all forms of pulmonary hypertension

Two chief types were recognised (1) multiple embolic carcinomatosis behaving like subacute thrombo embolic pulmonary hypertension as in the case described by Mason (1940) which was secondary to carcinoma of the breast, (2) diffuse lymphatic carcinomatosis with secondary thrombosis of the small pulmonary arteries and arterioles as in the case described by Brill and Robertson (1937) in which carcinoma of the stomach was responsible

Of four cases of my own however none presented like subacute pulmonary hypertension but all had the features of subacute cor pulmonale with doubtful or absent central cyanosis at rest marked breathlessness and central cyanosis on effort, and a remarkably hyperkinetic circulation ending in congestive heart failure Only the last of these four was investigated physiologically and at the time clinical heart failure was present Both right and left atrial pressures were raised the right being 8/ 1 with reference to the sternal angle with *a* and *v* about equal in amplitude and the left being 15/5 with *v* dominant The pulmonary artery pressure was 45/20 the right ventricular pressure 45/0/8 the cardiac output 7 3 litres per minute the pulmonary vascular resistance only 2 units and the arterial oxygen saturation 83 per cent A low hæmoglobin (59 per cent) prevented central cyanosis at rest as it may often do in this group These findings excluded obstructive pulmonary hypertension At the time these four cases were seen it was not at all clear what was causing the central cyanosis for there was no evidence of emphysema There seems little doubt in retrospect that they were suffering from a diffusion difficulty and that physiologically they resembled cases with diffuse interstitial fibrosis The case investigated showed diffuse lymphatic spread from a bronchial carcinoma of the right middle lobe bronchus (fig 19 10) Of the other three cases the primary growth was in the stomach in one in the breast in one and was not established in the third



Fig 19 10—Subacute anoxic cor pulmonale with heart failure and a normal pulmonary vascular resistance due to diffuse lymphatic carcinomatosis secondary to bronchial carcinoma

Of four cases described by Storstein (1951) two were secondary to carcinoma of the stomach and two to carcinoma of the breast Physiological investigations in two of the cases revealed pulmonary artery pressures of 36/17 and 26/7 cardiac outputs of 5 and 4 litres per minute

pulmonary vascular resistances of about 4 and 3 units and arterial oxygen saturations at rest of 78 and 61 per cent respectively

Reporting 24 new cases of this condition and reviewing 154 from the literature Harold (1952) gives its frequency as 1 5 per cent of 836 con*secutive necropsies at St Bartholomew s Hospital, or 7 5 per cent of* all cases of malignant disease The essential pathological findings were distension of the peribronchial and perivascular lymphatics by tumour cells with secondary interstitial fibrosis intravascular tumour emboli *secondary thrombosis and obliterative endarteritis were seen occasionally* Of the total of 178 cases the primary tumour was gastric in 53 5 per cent bronchial in 13 per cent mammary in 9 5 per cent pancreatic in 6 per cent and prostatic in 4 per cent Although only one of Harold s 24 *cases collected* from the records at Brompton and St Bartholomew s Hospitals was recognised as having terminal subacute cor pulmonale his statement that the outstanding symptom was severe increasing breathlessness until the patient became distressed on the least exertion *leaves little room for doubt* as to what was happening physiologically It seems unlikely however that pulmonary hypertension was a feature of any of these cases

The clinical diagnosis is based on the combination of subacute hypoxic cor pulmonale usually without marked pulmonary hypertension the characteristic radiological changes of diffuse lymphatic carcinomatosis evidence of the primary neoplasm secondary anæmia instead of polycythæmia relatively good ventilatory function absence of carbon dioxide *retention and the demonstration of impeded oxygen diffusion*

The prognosis is hopeless and treatment can only be symptomatic

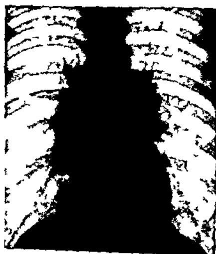
Honeycomb lung

The occurrence of small thin walled air containing cysts measuring up to a maximum of 1 cm in diameter and widely distributed throughout both lungs may be associated with interstitial fibrosis however caused (Oswald and Parkinson 1949) *Known forms of interstitial disease that* may develop these cysts include xanthomatosis (Rowland 1928) reticuloses in infants (Mallory 1942) tuberous sclerosis (Berg and Vejlens 1939) and probably diffuse interstitial fibrosis itself (*Oswald and Parkinson* 1949) A few may be congenital Bronchograms reveal no filling of the cysts with lipiodol but the frequency of pneumothorax, which is often recurrent and bilateral suggests some communication between some of the cysts and the bronchial tree The cysts are sometimes lined with flattened epithelium sometimes not Adjacent cysts are separated by thick walled septa which may contain connective tissue and blood vessels The bronchial tree itself appears to be normal

Physiological studies in this group are scanty There were only two examples in my series of 45 cases of chronic cor pulmonale *The first* was a cyanosed woman of 26 with an obviously hyperkinetic circulatory state who finally developed congestive heart failure opened up a valve patent

foramen ovale, and died from paradoxical cerebral embolism Her vital capacity was 2 litre her arterial oxygen saturation 72 per cent in an oxygen tent and from the modest (grade 2) electrocardiographic changes her pulmonary vascular resistance was probably between 6 and 9 units

The second case was a man of 28 admitted with congestive heart failure and typical radiological evidence of honeycomb lung (fig 19 11) The arterial oxygen saturation was 69 per cent cardiac output 4 4 litres per minute mean pulmonary artery pressure 43 mm Hg pulmonary vascular resistance 10 units and hæmoglobin 115 per cent The arterial carbon dioxide content was not estimated


Fig 19 11—Anoxic cor pulmonale with a high pulmonary vascular resistance due to honeycomb lungs

Necropsy confirmed the diagnosis in both these cases but whether the physiological behaviour was like emphysema or interstitial fibrosis cannot be determined from the inadequate investigations carried out at the time

Clinically the majority of patients with honeycomb lung who survive the pneumothorax hazard develop cor pulmonale sooner or later Anoxia and a hyperkinetic circulation are probably usual but the pulmonary vascular resistance may also be high Interstitial fibrosis is likely to impede oxygen diffusion across the alveolar capillary interface and perfusion of unventilated air containing cysts is likely to cause a high degree of venous admixture in the arterial blood

Ayerza s disease

Much confusion has arisen from the use of this term it has been applied to cases of intense cyanosis and polycythæmia associated with syphilitic or other disease of the pulmonary arteries (Boyd 1931) The facts are that Ayerza of Buenos Aires *in an unpublished clinical lecture* (1901) described a single case of heart failure *in which the* patient was so cyanosed as to be almost black—a *cardiac negro* Autopsy revealed much enlargement of the right side of the heart dilatation of the bronchi and peribronchitis Neither syphilis nor the state of the pulmonary vessels was mentioned Arrillaga (1913 1924) was perhaps chiefly responsible for stressing the syphilitic origin of such cases although other authors from the Argentine believed the arterial lesions to be atherosclerotic Brenner (1935) after reviewing the evidence concluded that there was no goo

reason for retaining the term Ayerza's disease on the grounds that published cases described nothing but chronic cor pulmonale

Cor pulmonale associated with deformities of the chest

Gross kyphoscoliosis accounts for perhaps 1 5 per cent of cases of chronic cor pulmonale The condition is associated with extensive collapse atrophy of part of the lung and severe emphysema of the remainder Cardiovascular involvement is similar in type to that associated with other forms of emphysema kinking of the aorta (Corvisart) plays no part in its development*

A curious form of syncope has been described in a number (Chapman Dill and Graybiel 1939) possibly due to sudden lowering of the right atrial pressure consequent upon compression of the inferior vena cava in certain postures (page 13) Otherwise the symptoms are similar to those of cor pulmonale from ordinary emphysema There is also the same tendency to chest infection

On the average death occurs five months after the onset of heart failure and at an average age of 30 years An injection of morphine is particularly lethal (Fischer and Dolelude 1954)

Aneurysm of the pulmonary artery

Aneurysm of the pulmonary artery is rare being found in less than 0 1 per cent of all autopsies and accounting for less than 0 5 per cent of all aneurysms (Deterling and Clagett 1947) The sexes are represented equally and about one third of the patients are under 30 years of age (Boyd and McGarack 1939) The etiology is believed to be a congenital defect in the wall of the pulmonary artery in about 40 per cent syphilis in 30 per cent and chronic cor pulmonale with atherosclerotic pulmonary arteries in 30 per cent The diagnosis may be obvious on fluoroscopy if gross pulsation is seen if not it may be proved by means of angiocardiography (Robb and Steinberg 1940)

In pulmonary heart disease aneurysmal dilatation may develop remarkably quickly underlying congenital weakness of the arterial wall is difficult to exclude Thrombosis may occur in the sac or the whole vessel may be occluded but apart from such a complication the aneurysm is unlikely to influence the course of the primary disease Rupture is very rare

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CHAPTER XX

THYROTOXICOSIS AND THE HEART IN MYXŒDEMA

THYROTOXIC HEART DISEASE

THE cardiovascular system is clearly involved from the onset of thyrotoxicosis although the term thyrotoxic heart disease is usually reserved for the late stage when auricular fibrillation or congestive heart failure dominates the scene Such a distinction is artificial and simply means that a young and healthy heart can maintain a high output for years without distress but that an aged heart cannot

Historical note Thyrotoxic heart disease was first adequately described by Caleb Hillier Parry (1815 1825) of Bath who witnessed his first case in 1786 Flajani s publication of the details of one case (1802) appeared first but cannot be compared with Parry s account Graves description (1835) is also inferior Carl von Basedow (1840) a general practitioner at Merseburg Germany, called special attention to exophthalmos and drew a vivid picture of most of the features of primary exophthalmic goitre as we see it today omitting only tremor which was later recognised and added to the Merseburg triad (exophthalmos goitre and palpitations) by Pierre Marie (1883) For further historical details the reader is referred to the classical monographs of Cecil Joll (1932) and of Means and Richardson (1938)

NATURE OF THYROID HORMONE

The exact composition of thyroid hormone is not yet known In 1895 Baumann obtained from thyroid tissue a protein free physiologically active substance containing 10 per cent of iodine which he called iodothyrin In 1899 Oswald showed that the active principle stored in the gland was attached to a protein in the form of thyroglobulin this is the chief constituent of colloid Kendall isolated thyroxine in 1915 showed that it contained 65 per cent of iodine and demonstrated its potency These researches culminated in the synthesis of thyroxine by Harington and Barger in 1927

Thyroxine however accounts for only 40 to 50 per cent of the total iodine in the thyroid gland is relatively insoluble and is not believed to be identical with thyroid hormone The rest of the thyroid iodine is found in the practically inert substance di iodotyrosine a likely precursor of thyroxine According to Harington (1933) thyroxine and di iodotyrosine are probably linked with amino acids as constituents of thyroglobulin in colloid and the natural thyroid hormone is perhaps a thyroxine containing peptide

PATHOLOGY OF GOITRE

The normal thyroid gland consists essentially of numerous acini lined with epithelium and containing colloid material rich in iodine from which thyroid hormone appears to be liberated according to the demand When the gland is stimulated the epithelium assumes an active columnar form and colloid tends to disappear When there is little or none left the walls of the acini may become crenated like any other vesicle whose contents have been removed In this phase the gland as a whole is soft and vascular and is not enlarged When the stimulus ceases involution takes place the epithelum flattens colloid reappears, and the acini become distended This is the resting phase and is characterised by a firmer less vascular gland of somewhat larger size If the stimulus to activity is excessive the morphological changes described above are supplemented by true hyperplasia of the acinar epithelium and subsequent involution may be incomplete leading to permanent enlargement of the gland

Simple goitre is due to benign hyperplasia and develops when iodine supplies are short or diverted especially when thyroid demands are heavy (Marine 1927) This response to iodine lack is believed by some to be mediated by the production of excessive amounts of thyrotropic hormone from the anterior pituitary Endemic goitre due to lack of iodine in the soil occurs in New Zealand parts of Italy and North America and in many other mountainous districts or places remote from the sea Iodine diversion may be due to polluted water (Marine and Lenhart 1910 McCarrison 1927) Increased demands for thyroid hormone occur at puberty and during pregnancy

Colloid goitre represents the resting involuted phase of previous benign hyperplasia (Marine 1930) When the stimulus subsides colloid reaccumulates in the acini intervening walls between distended crowded vesicles break down to form cysts and the whole gland becomes tense and big This process is innocent and causes no symptoms except possible discomfort in the neck

In primary Graves disease persistent uncontrolled stimulation of the thyroid gland of unknown cause leads to marked hyperplasia and to wild manufacture and liberation of excessive amounts of thyroid hormone The acinar epithelium is columnar and proliferated the walls of the acini markedly crenated and the colloid practically all gone The gland as a whole is soft vascular and enlarged

Nodular goitre is usually regarded as the end result of repeated cycle of hyperplasia and incomplete involution The process probably begins with failure of complete involution of a previously stimulated and hyperplastic gland Subsequent stimulation leads to local hyperplasia of these hypo involuted nests and subsequent involution to local nodules of colloid goitre Such a process may be repeated indefinitely Thyrotoxicosis from nodular goitre depends chiefly upon the activity of the hyperplastic nests the nodules themselves being mostly inert The term adenomatous goitre

is therefore incorrect when applied to this type of lesion and should be reserved to describe those cases in which thyroid nodules (usually single) are composed of solid masses of cells of fœtal type Compared with primary Graves disease nodular goitre usually runs a longer and less dramatic course which by its very nature is necessarily phasic periods of activity alternating with periods of relative quiescence Why production of thyroid hormone should exceed the demand is no more understood than it is in primary Graves disease The implication of the anterior pituitary thyro tropic hormone may explain part of the mechanism but in no way solves the problem

Physiology of the circulation under the influence of thyroxin The adminis tration of thyroxin to man and mammals is followed after a time lag of several days by an appreciable rise in the basal metabolic rate The in creased oxygen requirement is met by elevation of the cardiac output not by greater utilisation of available oxygen (as occurs when the B M R is raised by dinitrocresol) nor by polycythæmia The high minute output is maintained more by tachycardia than by a raised venous pressure the stroke volume being but little increased (Friedberg and Sohval 1937) The strength of cardiac contraction is probably enhanced These effects are usually attributed to the direct action of thyroxine on the heart

At the same time the peripheral blood flow is greatly increased there is obvious vasodilatation in the skin and adrenergic responses are magnified

Morbid anatomy of the thyrotoxic heart There are no macroscopic changes in the thyrotoxic heart prior to the onset of auricular fibrillation and failure until then the heart weight remains normal Cases exhibiting cardiac em barrassment during life may still show little at necropsy except some increase in heart weight and evidence of congestive failure (Kepler and Barnes 1932) In a few however there are scattered foci of fibrosis (Rake and McEachearn 1932)

CLINICAL FEATURES

The hyperkinetic circulation of primary Graves disease is usually well tolerated because the subjects are young but in middle aged or elderly people with toxic nodular goitre cardiac embarrassment is the rule The sex ratio favours women in the proportion of about 6 1 (Fraser and Dun hill 1934) A family history of goitre is found in 45 per cent of cases (Bruun 1945) Contributory factors include pregnancy the climacteric infection (such as tonsillitis) and perhaps emotional shock although the scarcity of thyrotoxicosis amongst active service casualties in the first two world wars was noteworthy The role of iodine has already been discussed

Of the symptoms loss of weight heat intolerance agitation or restless ness palpitations and fatigue are the most important Loss of weight as sociated with a voracious appetite is particularly suggestive Palpitations may be due to vigorous and rapid action of the heart or to paroxysmal auricular fibrillation the latter is especially significant

Whilst the symptoms themselves are important the manner in which they are told and the general behaviour and appearance of the patient are often more so The subject is usually a woman she is commonly thin and talks quickly often gesticulating to lend emphasis to her remarks She may wear a scarf to hide an unsightly swelling in her neck but her clothing is otherwise light One of Parry s patients liked to sit in a draught stripped to the waist in order to keep cool (Parry 1815) A good moment to look for the goitre is towards the beginning of the interview when the patient may lean forward in her chair and swallow once or twice in nervousness The eyes are characteristic not so much because of exophthalmos which is usually absent but because of their typical stare The trend of the patient s conversation is often illuminating and in sharp contrast to that of the anxiety neurotic The latter complains of symptom after symptom in a challenging fashion exaggerating their severity and stressing his inability to cope with them The thyrotoxic patient tries to explain away her symptoms she feels the heat but of course it has been very warm recently she is losing weight but she supposes she was too fat before she gets tired and irritable but she knows she tries to do too much and so on

Physical examination may reveal a wealth of signs which are all directly or indirectly attributable to excess of thyroid hormone except exophthalmos and goitre They may be suitably described under four main headings

1 *The eyes* Exophthalmos may be present (fig 20 01) but is uncommon in toxic nodular goitre It is occasionally unilateral (fig 20 02) Artificial glass eyes may also become proptosed Its mechanism is still a subject of controversy (Zondek and Ticho 1945) but exophthalmos is certainly not due to sympathetic stimulation, for it is not relieved by sympathectomy (Shaw 1949) nor is it due to excess of thyroid hormone which never reproduces it Moreover exophthalmos occasionally becomes more marked after thyroidectomy or treatment with thiouracil In severe cases of exophthalmic ophthalmoplegia and malignant exophthalmos, thyrotoxicosis may be minimal and the protrusion of the eye ball appears to be secondary to intense oedema of the orbital contents (Brain and Turnbull 1938) Of great interest is the exophthalmos that can be produced in guinea pigs (also in rabbits and fish but not so far in man) by injecting thyrotropic hormone especially if the thyroid gland is first removed (Marine and Rosen 1933) All these facts point to the likelihood of the pituitary being directly responsible and provide further evidence that thyrotoxicosis may depend upon a primary pituitary disorder

Retraction of the upper lid (fig 20 03) revealing the white sclerotic above the iris (Dalrymple s sign), which may be unilateral is also uncommon in toxic nodular goitre It should be distinguished from exophthalmos which reveals the white sclerotic below the iris by mechanically displacing the lower lid (Pochin 1937-8)

If the patient looks up and then lowers the eyes to watch a descending object the upper lid lags behind the movement of the eye ball revealing



(a)

Fig 20 01—Exophthalmic goitre The first photograph (a) (in gipsy dress) was taken in 1933 the second (b) in 1936 The white sclerotics are seen below the iris due to mechanical displacement of the lower lid



(b)

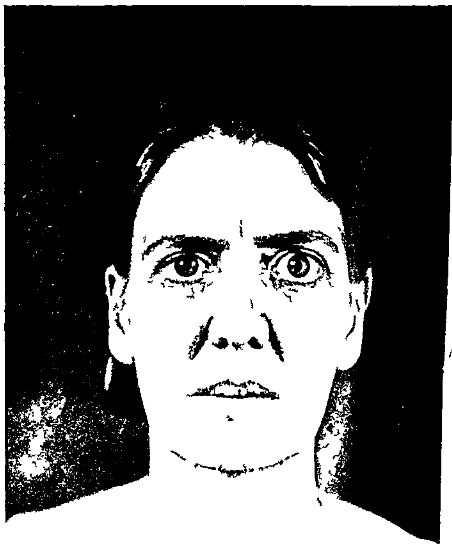


Fig 20 02—Unilateral lid retraction and exophthalmos

Fig 20 03—Lid retraction and characteristic thyrotoxic stare



the white sclerotic above the iris (von Graefe 1864) Lid lag and lid retraction were for a long time attributed to stimulation of the sympathetic reinforcement of the levator palpabræ superioris (von Graefe 1864) but if sympathetic stimulation were responsible the lower lid would also be retracted which it is not (Pochin 1937–8, 1939) Moreover, both exophthalmos and lid retraction may occur when the ocular sympathetic is paralysed (Brain 1939) In the light of these findings von Graefe s hypothesis is untenable

The characteristic stare has already been mentioned It is more than lid retraction and infrequent blinking (Stellwag s sign) it is a look which may occur independently and which can be recognised with experience The other eye signs of the textbooks are less important failure to wrinkle the forehead when the eyes are cast up (Joffroy s sign) may depend upon lid retraction and exophthalmos divergent strabismus as the eyes focus on an approaching object (Moebius sign) may be due to weakness of the oculomotor muscles as a result of stretching

2 *The hands* The hands are warm pink and slightly moist on both surfaces they are restless and expressive and may show a fine even constant tremor In contrast the hands of a psychoneurotic are cold and clammy being wet on the palms but not at the back they tend to be inert and expressionless tremor is coarse irregular and inconstant



Fig 20 04—Substernal goitre revealed by X rays

3 *The goitre* If a goitre is not seen it may be discovered by palpation It is best to stand behind the patient and to place the thumbs behind the sterno mastoids and the fingers in front On asking the patient to swallow a nodular swelling may be felt moving upwards Posterior enlargement may be detected readily with this technique Practically all cases of thyrotoxicosis have a goitre although it is sometimes difficult to demonstrate (so called masked hyperthyroidism) In such instances it may become more convincing after a course of Lugol s iodine Occasionally it is substernal and may be revealed by fluoroscopy (fig 20 04)

The goitre of thyrotoxic heart disease is commonly nodular irregular and asymmetrical It may displace the trachea to one side and the common carotid artery to the other and on rare occasions it may compress the trachea causing cough dyspnœa and stridor Sudden enlargement is usually due to hæmorrhage within [illegible] or cyst Degenerated nodules may become calcified

Primary exophthalmic goitres are uniformly enlarged smooth and fleshy

They are similar to simple hyperplastic goitres but more vascular Some times an arteriovenous continuous thrill and murmur may be detected over the gland Colloid goitres are also smooth and symmetrical but they are harder and as a rule larger After a course of iodine primary exophthalmic goitre may feel like colloid goitre Nodular goitre should be distinguished from other causes of thyroid enlargement and from other swellings in the neck

Fœtal adenoma (Wolfler 1883) whether regarded as a true neoplasm arising in nests of embryonic epithelial cells or as an ordinary hyperplastic nodule in which the vesicles are unusually small and devoid of colloid (Joll 1932) presents clinically as a firm smooth single tumour within the sub stance of the thyroid gland It is usually innocent

What were believed to have been *malignant changes* were found by Wilson (1921) and by Speese and Brown (1921) in about 5 per cent of all goitres that were surgically removed but their histological criteria have been dis puted and the true incidence of malignancy is probably lower In non toxic goitres it may be between 1 and 4 per cent (Lerman 1944) but in toxic nodular goitre it is extremely rare Thus Means (1937) said he had not seen a single case and Crile (1936) met no instance of toxicity amongst 249 malignant cases Malignancy should be suspected when a goitre grows rapidly becomes unduly hard causes dysphagia involves the recurrent laryngeal nerve, surrounds and buries the common carotid artery obstructs the internal jugular vein causes pain by involving adjacent sensory nerves or when fixation can be demonstrated Enlargement of neighbouring cer vical lymph glands is particularly suggestive Metastases are found espe cially in the lungs and bone

Riedel s disease (Riedel 1896) may be readily confused with malignant disease clinically It is characterised by a brawny induration of part or all of the thyroid gland sometimes involving surrounding tissues It is a slow fibrotic process of unknown ætiology affecting individuals of either sex and of any age Pain dyspnœa dysphagia huskiness of the voice and obstruc tion of neighbouring vessels occur and the gland is soon fixed but lymph nodes are not enlarged and thyrotoxic symptoms are unusual

Lymphadenoid goitre (Hashimoto s disease) is seen particularly in women over the age of 45 The whole gland is involved from the start surround ing structures *are not affected* and myxœdema usually develops (Joll 1932) Microscopically acinar remnants are scattered among masses of lymphoid tissue

Acute thyroiditis may complicate a variety of infections but is rare It may be suppurative or non suppurative according to the nature of the in vading organism and to the severity of the attack Clinically it is charac terised by a painful tender uniform swelling of the gland accompanied by fever Cellulitis with or without suppuration may invade surrounding tis sues Thyrotoxic symptoms may be associated but usually subside with the inflammation

Thyroglossal cyst is essentially a mid line structure developing from remnants of the thyroglossal duct, and moves upwards when the tongue is protruded It is of cosmetic rather than medical significance

4 *Cardiovascular signs* Vasodilatation in the skin and muscle is nearly always present and may be recognised by hot extremities distended fore arm veins throbbing digital vessels capillary pulsation modified water hammer pulse and raised pulse pressure Tachycardia is the rule and persists during sleep (Boas, 1932) The action of the heart is vigorous the cardiac impulse being forceful and displaced a little to the left, and the heart sounds slapping A systolic murmur may be heard at apex or base and a thrill may be felt on compressing the carotid or subclavian artery Rarely a functional mitral diastolic murmur may be heard

Auricular fibrillation may be initiated by overdosage of thyroxine in patients with normal hearts It occurs in 10 per cent of all cases of thyrotoxicosis and in 84 to 96 per cent of those with cardiac failure and may be paroxysmal or persistent It is rare in young subjects but becomes progressively frequent with advancing years During attacks the ventricular rate is apt to be very fast and the patient may complain of violent palpitations



Fig 20 05—Skiagram showing slight prominence of the aortic knuckle and of the left pulmonary arc in a case of thyrotoxicosis

Cardiac enlargement and failure are also relatively late developments and are unusual with normal rhythm but often follow the onset of auricular fibrillation An appreciable proportion of such cases (over 50 per cent according to Magee and Smith 1935) are complicated by hypertension or other forms of heart disease

X rays may show slight prominence of both the aortic knuckle and left pulmonary arc (Parkinson and Cookson 1931) and general fullness of all chambers probably due to the high cardiac output (fig 20 05) The electrocardiogram may be within normal limits unless it shows auricular fibrillation or the voltage of *P* and *QRS* may be augmented (fig 20 06)

5 *Other and less constant features* Neurological signs are rare they include exophthalmic ophthalmoplegia and myasthenia—sometimes resembling myasthenia gravis but not responding to prostigmine Curious-

patches of local myxœdema occasionally occur on the legs koilonychia has been described and the skin may be unduly pigmented

Decalcification of bone is not uncommon a negative calcium and nitrogen balance may be demonstrated the blood cholesterol may be rather low sugar tolerance may be reduced and impairment of hepatic function has been reported

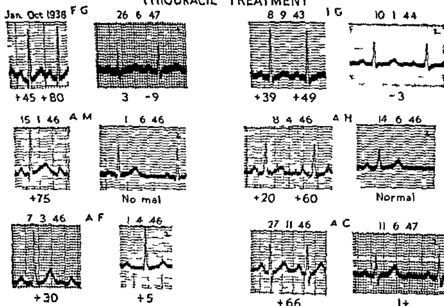


Fig 20 06—Ele trocardiog ams (all lead 2) showing relatively high voltage P and QRS waves in 6 ases of thyrotoxico is After treatment with thiouracil the voltage falls considerably The B M R is recorded und r each record

SPECIAL INVESTIGATIONS

1 *The basal metabolic rate* (B M R) introduced by Magnus Levy in 1895 has proved a useful guide to the degree of hyperthyroidism and is a measurement of the amount of oxygen consumed by the patient per minute when at complete rest i e fourteen hours after the last meal and after lying down undisturbed for at lea t half an hour The patient breathes in and out of a closed system containing equal proportions of air and oxygen for ten minutes carbon dioxide being removed by means of soda lime the amount of gas disappearing from the system represents the total amount of oxygen consumed This is then recorded in terms of oxygen consumption per square metre of body surface per minute and expressed as a percentage of what a normal person of the same age and sex would require In thyrotoxicosis the B M R commonly ranges between plus 10 and plus 80 per cent Read s formula for estimating the B M R by the pulse rate and pulse pressure is unreliable and worth no more than the knowledge that the com

bination of tachycardia and a bounding pulse suggests a raised cardiac output (Read s formula is B M R equals ¾ [pulse rate plus ¾ pulse pressure] minus 72)

It should be understood that a single B M R of plus 20 per cent does not necessarily mean that the disease is milder than one with a B M R of plus 40 per cent for the course of thyrotoxicosis is variable Serial readings may give a truer picture of the degree of activity Another important point is that auricular fibrillation and heart failure are more often associated with low grade activity acting over a long period of time, than with acute thyrotoxicosis so that the level of the B M R is no guide to the degree of cardiac disability

The B M R is more difficult to interpret when measured for diagnostic purposes but if it is below plus 10 per cent thyrotoxicosis is improbable High readings however may be due to faulty basal conditions o to other causes such as leukæmia and relatively high readings may be obtained in congestive heart failure of any etiology According to Foote *et al* (195) 23 per cent of thyrotoxic patients have basal metabolic rates within the normal range

2 *The administration of* 10 *minims* (0 6 *ml*) *of Lugol s iodine* three times daily for a week or ten days may be used as a test for hyperthyroidism in two ways (1) to see whether it unmasks a goitre, for a hyperplastic gland enlarges and hardens under its influence (2) to determine its effect on the sleeping pulse body weight and B M R for these are beneficially influenced in thyrotoxic cases but not when the B M R is raised from other causes

3 *Measurements of the cardiac output peripheral blood flow and circulation time* provide valuable data Outputs of 8 to 12 litres per minute are usual and are correlated more with the heart rate than with the venous filling pressure When the heart fails the output drops usually to subnormal levels The fore arm blood flow is invariably increased and usually remains so when the cardiac output falls as a result of failure moreover the augmented flow does not subside for several weeks after the B M R has been restored to normal by means of thyroidectomy or thiouracil therapy (Howarth 1948) Circulation times under 10 seconds are characteristic (Goldberg 1938) and may remain well within normal limits when there is systemic congestion

The demonstration of a high cardiac output at rest places a case in the hyperkinetic group the differential diagnosis then includes severe anæmia anoxic cor pulmonale arterio venous aneurysm Paget s disease of bone secondary carcinoma involving the liver or other serious hepatic disorders and beri beri The majority of these can be recognised or excluded at once on clinical grounds

4 *Urinary creatine test* Up to 200 mg of creatine may be excreted daily in the urine by normal women and children in an irregular manner but very little if any by normal men Excessive creatinuria occurs during

pregnancy and increased amounts may appear in the urine of either sex in fevers wasting diseases and certain muscular dystrophies

Most thyrotoxic subjects excrete an excess of creatine (Sohval King and Reiner 1938) and its detection may be used as a diagnostic test if the above considerations are borne in mind Thyroid responsibility may be proved by the disappearance of creatinuria within ten days of first giving iodine or thiouracil treatment (fig 20 07) (Schrire 1938) On the other

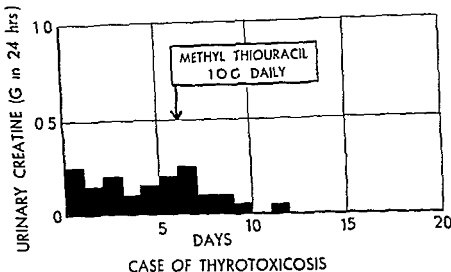


Fig 20 07—Effect of thiouracil on the excretion of creatine in the urine

hand, absence of creatinuria does not exclude thyrotoxic heart disease, for such cases are apt to be associated with low grade toxicity acting over a long period of time rather than with a high degree of hyperthyroidism and creatine excretion may be well within normal limits

5 *Electrocardiography* may reveal abnormally high voltage of P and QRS (fig 20 06) as previously stated It may also be of value in proving the nature of an irregularity of rhythm or in excluding certain other causes of a hyperkinetic circulation (e g pulmonary heart disease and anæmia)

6 *Radioactive iodine* (I^{131}) which has a half life of eight days may be given orally or intravenously in single test doses of 10 to 30 microcuries to see how the thyroid gland deals with it (Keating *et al* 1945) The body does not distinguish between radio iodine and ordinary iodine The concentration of I^{131} in liquids such as the plasma and urine can be estimated by means of liquid counters that detect the beta ray emanation the concentration of I^{131} in any tissue zone can be estimated by means of surface Geiger Muller counters that detect gamma rays which unlike the soft beta rays penetrate the skin Normally the concentration of I^{131} in the thyroid gland reaches a maximum of about 33 per cent of the test dose in two or three days and then slowly declines (Myant and Pochin 19

Simultaneously about 60 per cent of the test dose is excreted in the urine within two days, the actual quantities extracted by the thyroid or excreted in the urine depending on the concentration of I^{131} in the plasma The plasma concentration necessarily falls to a very low level by the end of the second day for 93 per cent of the test dose is by then in the thyroid gland or excreted in the urine Subsequently however I^{131} again appears in the plasma as protein bound radiothyroxine The more active the thyroid gland the greater the quantities of iodine extracted and radiothyroxine manufactured the quicker the turn over and the less iodine excreted in the urine (Myant and Pochin 1949) the more inactive the gland the more does the reverse hold true

All radioactive iodine tests of thyroid function are based on these four fundamental principles

(i) *The concentration of I^{131} in the thyroid gland* at the end of four hours in normal subjects averages 20 to 25 per cent of a 10 microcurie *test* dose (range 10 to 40 per cent) in thyrotoxicosis it is usually 40 to 90 per cent (Wayne 1954) This type of test is sometimes expressed as a neck/thigh ratio the concentration of I^{131} in the thigh serving as a control so that the amount of iodine in the thyroid gland can be distinguished from the amount in the soft tissues of the neck (Pochin 1950)

(ii) Thyroxine as manufactured and released by the thyroid gland is closely bound to protein and when circulating in the plasma may therefore be precipitated with the plasma proteins Radiothyroxine of course is similarly protein bound As stated above the amount of protein bound radiothyroxine circulating in the plasma 24 to 48 hours after a 25 micro curie test dose of I^{131} is negligible in normal subjects being less than 0 4 per cent of the test dose per litre of plasma at the end of 48 hours and usually less than 0 1 per cent (Goodwin *et al* 1951) in thyrotoxicosis however it ranges between 0 04 and 3 5 per cent per litre (Wayne 1954)

(iii) The *thyroid clearance* test is the best measure of the speed at which the thyroid gland extracts iodine from the plasma After an intravenous test dose of 30 microcuries of I^{131} the thyroid gland normally extracts about 6 per cent of the test dose per hour when the plasma concentration is around 4 per cent of the test dose per litre this means that 1 5 litres of plasma are cleared of radio iodine per hour or that the thyroid clearance is 25 ml per minute *In* normal subjects the thyroid clearance ranges between 7 and 42 ml per minute *In* thyrotoxicosis however iodine extraction is speeded up and the thyroid clearance averages 240 ml per minute ranging between 80 and 500 (Pochin 1950)

(iv) *The quantity of I^{131} excreted in the urine* is proportional to its con centration in the plasma provided renal function is unimpaired Normally over 40 per cent of a 10 microcurie test dose is excreted in 24 hours whereas in cases of thyrotoxicosis less than 25 per cent is usually excreted in this time (Pochin 1950) This test is an indirect measure of the amount of I^{131} extracted by the thyroid gland during the 24 hours for the more

extracted the lower the plasma concentration and therefore the less excreted in the urine Mason (1949) and Fraser *et al* (1953) have shown that the urinary excretion test is more helpful if the amount of I[131] excreted during the first six or eight hours is considered separately for excretion is only diminished when the plasma concentration has fallen owing to increased thyroid extraction In practice the amount of I[131] excreted from the sixth or eighth to the twenty fourth hour after the test dose seems to be the most sensitive index of thyroid activity In normal subjects Mason (1949) found that 10 to 25 per cent of the test dose was excreted during the critical 6 to 24 hour period whereas in cases of thyrotoxicosis less than 4 5 per cent was excreted during this time

According to Wayne (1954) the most reliable of these tests is the estimation of protein bound radiothyroxine in the plasma at 48 hours thyroid clearance coming second and the amount of I[131] taken up by the thyroid gland in four hours third

TREATMENT

The most satisfactory method of treating thyrotoxic heart disease is subtotal thyroidectomy as developed by Dunhill (1908 1929 1937) The best results are obtained when physician and surgeon work in the closest harmony success depending as much upon the skill and judgment of the physician as upon the experience and dexterity of the surgeon (Fraser and Dunhill 1934) adequate premedication being all important

The patient should be put to bed and fed on a liberal and nourishing diet The addition of 5 to 10 mg of aneurin daily may be helpful on the grounds that an abundant supply of this vitamin is needed for the increased carbohydrate metabolism Fatigue and weakness may respond to 50 mg of pyridoxine daily (So kin and Levine 1944) Phenobarbitone ½ a grain (32 mg) t d s or potassium bromide 10 grains (0 64 G) t d s may also be prescribed with benefit and a nocturnal sedative is usually necessary

During this preliminary stage of treatment which usually induces some remission of symptoms the degree of thyrotoxicosis may be assessed clinically and by means of the special tests detailed above Prior to the introduction of thiouracil and the newer antithyroid drugs iodine was then given by mouth in doses of 10 minims (0 06 ml) of Lugol s solution three times daily preferably in milk Within ten days there was usually marked improvement the pulse rate fell the B M R was lowered and the patient felt better (Waller 1914 Plummer 1923) The moment for operation was usually ten to fourteen days after beginning iodine Nowadays however preliminary treatment with antithyroid drugs is preferred (*vide infra*)

The introduction of thiouracil by Astwood (1943) following the discovery by the Mackenzies (1941) that the administration of sulphaguanidine to rats caused thyroid hyperplasia and reduction of colloid has proved an important therapeutic advance Thyroid hyperplasia was attributed to increased production of thyrotropic hormone by the anterior pituitary

endeavour to compensate for deficiency of thyroid hormone brought about by sulphaguanidine Astwood found that many substances had a similar effect including all the sulphonamides, *p* aminobenzoic acid thiourea and its compounds and that of these thiouracil offered the best prospects being potent and relatively non toxic It is held that thiouracil and the other substances mentioned act by interfering with the union of iodine and tyrosine and so prevent the formation of di iodotyrosine a known precursor of thyroxine (Riker and Wescoe 1945) The histological appearance of the thyroid gland under their influence resembles the hyperplastic gland of iodine deficiency

Since then several other more potent and less toxic antithyroid drugs have been developed and several of them have superseded thiouracil These include methylthiouracil propylthiouracil and neomercazole The initial dose of thiouracil and its derivatives is 50 to 100 mg three times daily for two weeks followed by 25 to 50 mg two or three times daily thereafter (Astwood 1949) Neomercazole (Lawson *et al* 1951) is in a different category the equivalent dose being only 10 mg two or three times daily initially and 5 mg once or twice daily for maintenance

Extensive trials have established what may be expected from treatment with antithyroid drugs (Astwood 1944 Williams 1944 1946 Himsworth 1948 Goodwin *et al* 1954) Amelioration of all symptoms except exophthalmos and those due to the size of the goitre and objective evidence of reduced thyroxine output can be demonstrated in 90 per cent of cases but when the drug is withheld after a year or so there is a 2 1 chance in favour of relapse within forty eight months (Goodwin *et al* 1954) Moreover toxic symptoms such as fever, dermatitis purpura, adenopathy and agranulocytosis which develop in 13 per cent of cases having thiouracil (Van Winkle 1946) prevent long term treatment even with the less toxic propylthiouracil or neomercazole in about 5 per cent of cases The mortality from agranulocytosis due to thiouracil is 0 5 per cent (Moore 1946) Increasing exophthalmos and the development of a highly vascular expanding goitre are attributed to over activity of the pituitary thyrotropic hormone in response to subnormal thyroxine output and may be prevented by the simultaneous administration of a maintenance dose of *thyroid (Williams and Bissell 1943) or thyroxine (Fraser and Wilkinson* 1953)

Despite the high relapse rate antithyroid drugs may be the treatment of choice in acute cases of primary Grave s disease in young people *It is* usually unsatisfactory in the long run in well established cases of toxic nodular goitre relapse in this group being more or less inevitable when the drug is withheld

The antithyroid drugs however have proved invaluable for preparing patients for partial thyroidectomy and if l thyroxine sodium 0 1 to 0 3 mg daily or thyroid gr 1 to 3 daily is given in addition increased vascularity of the gland can be avoided Lugol s iodine may be used

instead of thyroid for the same purpose (Means 1946) but is probably less efficient The great advantage of the antithyroid drugs over Lugol s iodine in preparing patients for operation is the abolition of the sense of urgency, for patients do not relapse while taking antithyroid drugs

Cardiac complications do not contraindicate partial thyroidectomy (Dunhill 1937) More careful preparation however is needed auricular fibrillation must be controlled and heart failure relieved before it is safe to operate but normal rhythm should not be deliberately restored at this stage

The commonest post operative complication used to be paroxysmal auricular fibrillation with rapid ventricular rate but this is less frequent if the patient is prepared with an antithyroid substance It should not occasion undue alarm for the rhythm usually reverts to normal spontaneously within 48 hours If auricular fibrillation persists however whether previously well established or of recent onset every effort should be made to restore normal rhythm by means of quinidine before the patient leaves hospital The risk of embolism is slight perhaps because the hyperkinetic circulation lessens the chance of venous thrombosis

Treatment with radioactive iodine

Deep X ray therapy was curative in about a third of cases resulted in some improvement in a third and was without benefit in the remainder (Means and Holmes 1923) In the treatment of thyrotoxicosis it has now been wholly superseded by radioactive iodine

Radioactive iodine introduced as a potent therapeutic agent by Hertz and Roberts (1942 1946) has fulfilled its early promise (Chapman 1948 Prinzmetal *et al* 1949 Moe *et al* 1950) Until a sufficient number of patients have lived 20 years after the irradiation the risk of subsequent carcinoma cannot be accurately assessed In the meantime all workers are disinclined to advocate it in patients under 45 years of age with a life expectancy of at least 20 years In older patients in subjects with other diseases that have a relatively poor prognosis such as V D H or ischæmic heart disease when thyroidectomy is refused or considered too dangerous or when thyrotoxicosis has recurred post operatively radioactive iodine is the treatment of choice An absolute contra indication however, is pregnancy for the fœtal thyroid may concentrate I^{131} and be destroyed or seriously damaged

The therapeutic dose of I^{131} is approximately 100 to 200 microcuries per gram of estimated thyroid mass the exact dose depending upon the degree to which the gland concentrates radioactive iodine and the duration of its activity in the gland (Blomfield *et al* 1951)

The results of so treating 140 patients were reviewed after one year by Blomfield *et al* (1955) Symptoms usually abated within three to six months and finally 84 per cent became euthyroid myxœdema developed in 12 per cent and 4 per cent remained thyrotoxic There were no deaths

The thyroid gland usually became smaller in size and exophthalmos did not increase in the series reviewed (but may do so occasionally) The only side effect was rheumatism which occurred four to eight weeks after treatment in about 10 per cent of cases half of them non articular and recovering spontaneously

These results are impressive and certainly suggest that radioactive iodine would be the treatment of choice in all cases of thyrotoxicosis if the risk of subsequent carcinoma proves to be less than 2 per cent

Thyrotoxic crises Owing to the impossibility of neutralising thyroid hormone that has already been manufactured both iodine and thiouracil do not benefit the patient for several days (graphs illustrating the effect of partial thyroidectomy iodine and thiouracil on the basal metabolic rate are remarkably similar) The treatment of thyrotoxic crises by massive doses of iodine (by mouth or intravenously) as advocated by Boland and Kepler (1938) for example is therefore questionable Absolute rest heavy sedation and replacement of salt and water lost in sweating and vomiting are probably more important Aneurin, 100 mg. intravenously may also help

If toxic goitre is recognised and treated promptly however crises should not occur

Thyrotoxicosis and tonsillitis Cases are encountered in which an attack or repeated attacks of tonsillitis are associated with thyrotoxicosis The problem then arises whether to perform partial thyroidectomy or tonsillectomy first Before the introduction of thiouracil most authorities agreed that it was safer to remove the thyroid gland before the tonsils for tonsillectomy in thyrotoxic patients sometimes precipitated a crisis Thiouracil has simplified the problem however and allows tonsillectomy to be undertaken first without risk



Fig 20 08—Skiagram showing gross cardiac enlargement in a case of thyrotoxicosis plus mitral stenosis

Thyrotoxicosis and rheumatic heart disease Thyrotoxicosis may be associated with acute rheumatic carditis or with established rheumatic valve lesions Both Parry's and Basedow's first cases were so related The association if more than a coincidence is indirect and may depend upon their joint relationship to streptococcal tonsillitis Rheumatic heart dis

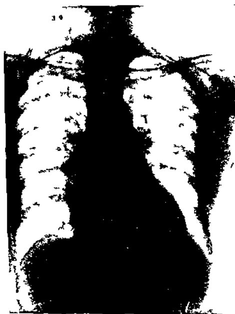
ease with fixed valve lesions may result in enormous enlargement of the heart owing to the excessive work induced by thyrotoxicosis (fig 20 08) and the sooner the latter is treated the better Radioactive iodine is ideal for these cases

Thyrotoxicosis and hypertension There is a group of cases sometimes designated thyrotoxic hypertension in which thyrotoxicosis is associated with high blood pressure both systolic and diastolic levels being raised There is little evidence of any direct relationship between the two diseases and the blood pressure does not fall following thyroidectomy (Bisgard 1939)

Thyrotoxicosis and angina pectoris Ischæmic heart pain occurs when the blood supply to the myocardium is insufficient to meet the demand By increasing the demand thyrotoxicosis may induce angina in a patient with



Fig 20 09 (a)—Thyrotoxic heart failure



(b)—After subtotal thyroidectomy

a relatively minor degree of coronary atherosclerosis behaving in this respect like anæmia Thyroid hormone also sensitises the organism to adrenalin When ischæmic and thyrotoxic heart disease are associated angina may be completely relieved at least temporarily by successful treatment of the thyrotoxicosis preferably by means of radioactive iodine

Thyrotoxicosis and pregnancy Thyrotoxicosis developing during pregnancy may be due to primary exophthalmic or nodular goitre With the aid of thiouracil in combination with small doses of iodine or thyroid patients should be taken safely to term If the condition does not then subside subtotal thyroidectomy may be carried out The danger of goitre

developing in the fœtus is minimised by the iodine (or thyroid) but it is well to keep the dose of antithyroid drug as small as possible

PROGNOSIS

There are few forms of heart disease that respond better to adequate treatment than thyrotoxic heart disease Cases with gross congestive failure and well established auricular fibrillation may be cured and the largest hearts may resume their normal size (fig 20 09) On the other hand heart failure and death are inevitable if the disease remains unchecked In the hands of the best surgeons the mortality rate of subtotal thyroidectomy in cases of toxic nodular goitre has been 1 6 per cent (Cole 1944) to 2 6 per cent (Dunhill 1937) but it may be less with thiouracil preparation No reliable figures are available upon which to assess the total relapse rate Post operative tetany and paralysis of the vocal cord each occurs in approximately 1 per cent (Means 1946)

Myxœdema which may follow otherwise successful treatment of thyrotoxicosis however accomplished is easily controlled by a maintenance dose of thyroid gr 3 or L thyroxine sodium 0 3 mg daily

THE HEART IN MYXŒDEMA

Artificial myxœdema produced by total ablation of the thyroid gland or by antithyroid drugs benefits the heart by lessening the circulatory demands and so relieves angina pectoris and congestive heart failure Yet well developed myxœdema from natural causes gives rise to cardiac enlargement pericardial effusion and ultimately to congestive heart failure moreover angina pectoris may be associated Enlargement cannot be due to overwork it must depend upon some intrinsic change in the heart muscle Histological examination however, is usually disappointing The fault is probably biochemical and is unlikely to be properly understood until studies in tissue chemistry are more advanced

The diagnosis of myxœdema is suggested by the placid sleepy character (unless there is manic psychosis) poor memory sensitivity to cold (Raynaud s phenomenon is common) dry coarse skin thickened lips and tongue low thick voice baggy eyes scanty dry hair podgy hands supraclavicular pads of fat and general pallor It is confirmed by an impalpable thyroid gland by a B M R of minus 30 to 40 per cent by prolongation of the arm to tongue circulation time to 19 to 25 seconds by a high blood cholesterol of 300 to 400 mg per cent by relative insensitivity to atropine and adrenaline by a characteristic form of anæmia and by a pathognomonic electrocardiogram If further proof is needed it may be obtained by demonstrating failure of the thyroid gland to extract radioactive iodine after a test dose so that the neck thigh ratio remains unaltered (Foote *et al* 1957) a thyroid clearance of only 1 to 4 ml per minute (Pochin 1950) or an abnormally high urinary excretion of radio iodine (Mason 1949 Fraser *et al*, 1953) Estimation of the protein bound radiothyroxine 48 hours

after a test dose of I^{131} does not distinguish myxœdema from normal controls (Wayne 1954)

The type of anæmia that responds to thyroxine alone is normocytic and orthochromic, and may be regarded as a compensatory adjustment to diminished oxygen requirement (Bomford 1938) The electrocardiogram shows sinus bradycardia low voltage atrial and ventricular complexes and flat or inverted T waves in all leads (fig 20 10) The cause of these changes is not yet understood they do not depend upon the presence of pericardial effusion nor upon the state of the subcutaneous tissues The response to thyroxine is quick and complete and accompanies beneficial changes in the B M R The electrocardiogram in cretinism behaves similarly (fig 20 11) (Schlesinger and Landtman 1949)

Whilst a well developed case of myxœdema is difficult to overlook (fig 20 12) cases of short duration especially in younger women (the sex incidence is 8 1 in favour of women) may easily escape notice The diagnosis should be considered in any case of congestive heart failure or of peri-

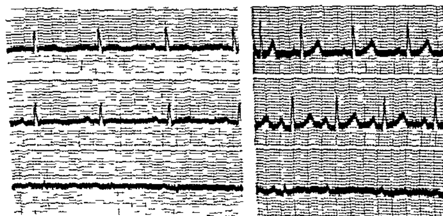
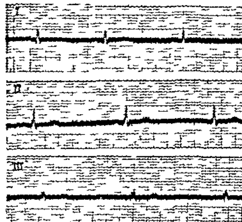


Fig 20 10 (a)—Electrocardiogram showing sinus bradycardia low voltage atrial and ventricular complexes and flat T waves in all leads in a case of myxœdema
(b) Normal electrocardiogram after treatment

cardial effusion of unknown etiology Congestion when it occurs is systemic and is associated with a low cardiac output Pericardial effusion is due to simple transudation Cardiac enlargement is general and pulsation of all chambers poor Angina pectoris has been said to occur in only 1 to 2 per cent of cases (Smyth 1938), but is surely much more frequent (Hueper 1944 1945) Coronary atherosclerosis may result from the high blood cholesterol Myocardial infarction without coronary thrombosis has been described in such cases when treated too vigorously with thyroxine The blood pressure is little influenced by myxœdema and is as often elevated as low When congestive failure is present measurements of the B M R give unduly high readings more reliance should then be on other tests, especially on the electrocardiogram



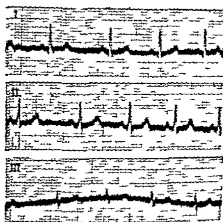


Fig 20 11—Electrocardiogram before and after trea ment in a case of cretini m



Fig 20 12 (a)—Myxœdema



(b) After seven weeks treatment.

Treatment If there is no evidence of coronary disease thyroxine may be given intravenously in a single dose of 10 mg or thyroid may be given by mouth in doses of 3 grains (0 2 G) daily The response is delayed but dramatic Within five to ten days the B M R rises the blood cholesterol falls the T wave begins to change and clinical improvement is obvious Signs of failure or of pericardial effusion soon disappear and the heart gradually resumes its normal size (Lerman Clark and Means 1933)

Initial treatment is easier than maintenance With the aid of the B M R it is not difficult to regulate dosage for a patient at rest in bed but when she leaves hospital and varies her activities it is not so easy and supervision is required for life The average maintenance dose of thyroid is 3 grains (0 2 G) daily by mouth or 0 3 mg of L thyroxine sodium

If there is any suspicion of associated coronary disease initial treatment should be cautious and the oral route advised Not more than 1 grain (65 mg) of thyroid should be given daily and in cases with angina pectoris not more than ½ a grain (32 mg) The dose may be increased slowly week by week if well tolerated or reduced and maintained at a minimum if not tolerated

The chief complication arising during treatment is the development of angina pectoris should this occur the dose of thyroid may have to be less than ideal but enough to keep the blood cholesterol below 300 mg per cent

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CHAPTER XXI

HYPERKINETIC CIRCULATORY STATES

(ANÆMIA PREGNANCY ARTERIO VENOUS FISTULA, BERI BERI PAGET S DISEASE OF BONE HEPATIC FAILURE)

IN addition to the diseases enumerated above hyperkinetic circulatory states (Harrison 1935) include thyrotoxicosis anoxic cor pulmonale fever and exercise The first two have been considered fully elsewhere and the last two have a purely physiological basis

All these conditions are characterised by a raised cardiac output maintained by means of tachycardia a raised venous filling pressure or both moreover the heart may beat more strongly Conspicuous evidence of vaso dilatation in skin and muscle is found in all of them the skin is warm and flushed the forearm veins are distended the pulse is bounding the digital vessels throb and there may be capillary pulsation The forearm and calf blood flows are increased Whilst young and healthy hearts may cope with the situation without distress older or unhealthy hearts may fail to meet the requirements The chief symptoms are palpitations and breathlessness

It may be difficult clinically to recognise congestive failure in these cases for the usual signs may have other interpretations Thus a raised venous pressure may be part of the physiological mechanism maintaining a high cardiac output (McMichael 1947) enlargement of the liver may be due to secondary carcinoma or to hepatitis and œdema is commonplace in severe anæmia and beri beri for other reasons Indeed it is by no means easy to be sure what is meant by failure in this group for example McMichael uses the term high output failure to describe a state in which a raised venous pressure and œdema are associated with a high cardiac output whether or not the latter is capable of being raised further Yet failure ordinarily denotes an overloaded heart or ventricle one incapable of raising its output further But this question has already been discussed (page 264)

THE HEART IN ANÆMIA

Physiology Severe chronic or post hæmorrhagic anæmia may affect the heart in three ways (i) it may cause a hyperkinetic circulatory state as described above (ii) it may cause or precipitate angina pectoris or acute coronary insufficiency (iii) it may result in nutritional degenerative changes in the cardiac muscle which may reduce its reserve

With an oxygen consumption of 240 ml per minute an anæmic subject with a hæmoglobin of 20 per cent could not have a cardiac output less th

6 litres per minute if all the available oxygen were utilised (20 per cent Hb = 3 G Hb per cent = 3 × 1 34 ml oxygen per cent = 4 ml oxygen per cent or 40 ml per litre Thus cardiac output = $\frac{240}{40}$ = 6 litres per minute) If half the available oxygen were utilised the cardiac output would be 1 litres per minute

In anæmic subjects investigations have shown that the resting cardiac output may reach 13 litres per minute and utilisation of available oxygen may be increased from the normal 33 per cent to as much as 90 per cent (Liljestrand and Stenstrom 1925–6 Nielson 1934 Sharpey Schafer 1944) These changes do not occur at rest with hæmoglobin values above 50 per cent but become increasingly apparent at lower levels (Bouchut and Froment 1934) The high cardiac output is maintained both by tachycardia and a raised venous pressure The latter must be due to widespread capillary or peripheral venoconstriction for the blood volume is reduced (McMichael *et al* 1943) and the small arteries and arterioles are dilated (McMichael 1947)

Clinical features The chief symptoms of severe anæmia are breathlessness fatigue and palpitations Angina pectoris occurs in about 30 per cent (Coombs 1926 Pickering and Wayne 1934) occasionally even when there is no underlying coronary disease Thus the author has treated a boy of 17 with pernicious anæmia and angina pectoris and also a young man of 21 who presented himself with classical ischæmic heart pain due to iron deficiency anæmia resulting from bleeding hæmorrhoids Œdema may be due to congestive heart failure but is more often nutritional It is especially prone to develop during the first three weeks of blood regeneration in response to treatment of the anæmia

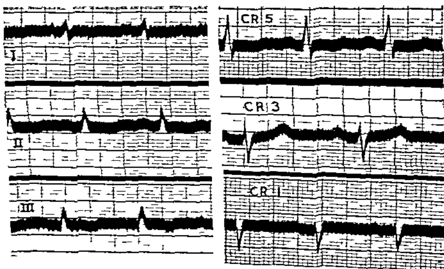
Paroxysmal cardiac dyspnœa or acute pulmonary œdema is rare as a spontaneous event but may arise during blood transfusion or saline infusion These procedures should not be lightly undertaken in cases of severe chronic or post hæmorrhagic anæmia precautionary measures include the use of concentrated red cells instead of whole blood and venous pressure lowering agents such as cuffs applied to the thighs Transfusion should be temporarily abandoned if the venous pressure is seen to rise appreciably

Physical signs A hyperkinetic circulation and peripheral vasodilatation may be recognised by the features detailed previously

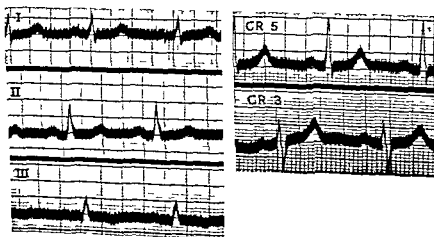
A functional systolic murmur (so called hæmic murmur) at apex or base is common and is due to the increased blood flow through the aortic and pulmonary valves Functional mitral or aortic diastolic murmurs may also be heard occasionally earlier observations such as those by Von Noorden (1891) Sahli (1895) and Kraus (1905) having been amply and repeatedly confirmed (Goldstein and Boas 1927) Mitral presystolic or diastolic murmurs are probably due directly or indirectly to the increased velocity of blood flow the mechanism being the same as that responsible for mitral

diastolic murmurs in patent ductus arteriosus ventricular septal defect and thyrotoxicosis Basal diastolic murmurs are attributed to dilatation of the aortic or pulmonary ring

The electrocardiogram Despite several publications emphasising the normality of the electrocardiogram in anæmia (e g Smith 1933 Pickering and Wayne 1934) there can be no doubt that significant changes occur in at least a third of cases with hæmoglobin values under 40 per cent (Block, 1937) In a consecutive series of twenty such cases analysed by the author



(a)



(b)

Fig 21 01—Electrocardiogram showing low voltage and flat or inverted T wave in all leads in a case of pernicious anæmia

(a) Before treatment

(b) After correction

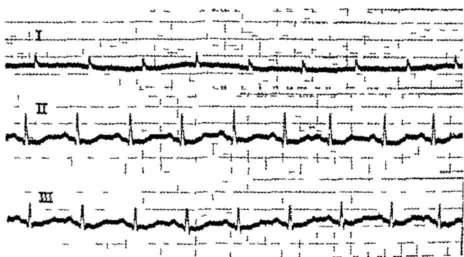


Fig 21 02 Electrocardiogram showing depression of the ST segment due to acute coronary insufficiency resulting from post hæmorrhagic anæmia

(a) Before treatment

(b) After treatment of the anæmia

Fig 21 03—Skiagram showing general cardiac enlargement in a case of severe pernicious anæmia

eight showed low voltage depressed S T segments or flat or inverted T waves in left ventricular surface leads or their equivalents As the anæmia improved under treatment these faults were corrected (fig 21 01) Several instances of bundle branch block have also been observed but these have always persisted when the anæmia was cured Depression of the S T segment is common following gross hæmorrhage and is believed to represent temporary coronary insufficiency (fig 21 02)

Fluoroscopy X rays often reveal slight enlargement of all chambers of the heart and prominence of both the aorta and pulmonary artery in cases with hæmoglobin levels below 40 per cent (fig 21 03)

Necropsy studies have revealed slight increase of heart weight (350 to 450 G) in the majority of cases of severe anæmia and considerable increase occasionally (Cabot and Richardson 1919) Experimental anæmia in rats has resulted in slight cardiac hypertrophy at hæmoglobin levels of 10 G per cent and considerable hypertrophy (weight at least twice normal) at levels of 2 to 3 G per cent (Forman and Daniels 1930–1) According to Grunberg (1930) hypertrophy is invariable in man when the hæmoglobin is 15 per cent or less and does not occur at all when the hæmoglobin is 66 per cent or more

These findings harmonise with the behaviour of the cardiac output in relation to hæmoglobin levels and there can be little doubt that enlargement depends on increased work

Clinical diagnosis Knowledge of cardiovascular behaviour is of little value in making a diagnosis of anæmia and is of no value at all in determining the nature of the anæmia It is helpful however in differential diagnosis especially between anæmia the anxiety states and bacterial endocarditis Thus an anxiety state may present with the same group of symptoms including pallor and there may be cardiac over action and functional systolic murmurs The pallor however, is due to peripheral vasoconstriction and does not affect the conjunctivæ or the mucous membranes and it is less obvious in the palms of the hands the nail beds too are more likely to be cyanosed than pale In anæmia pallor is often waxy chalky or lemon tinted according to its severity and type The cardiovascular dynamics are quite different Over action of the heart and tachycardia in the anxiety states are associated with little or no rise in cardiac output there is peripheral vasoconstriction rather than vasodilatation and the diastolic blood pressure tends to be raised in casual readings the stroke volume tends to be reduced and the pulse may be small the circulation time and venous pressure are normal There are however exceptions to this general pattern about 10 per cent of patients with an anxiety state having a hyperkinetic circulation probably caused by an excess of circulating adrenaline

A type of case that may cause confusion is one that presents with pallor low grade fever petechiæ splenomegaly over action of the heart and a loud systolic murmur at apex or base Bacterial endocarditis may be sus

pected especially when there is a diastolic basal murmur as well and the pulse is collapsing yet all these features may be due to anæmia alone

Treatment All cardiovascular changes due to anæmia are reversible if the anæmia is treated successfully Cardiac remedies are rarely required apart from urgent measures in the event of acute pulmonary œdema The danger of ill judged or too rapid intravenous infusion has already been mentioned

THE HEART IN PREGNANCY

PHYSIOLOGY

There is now sufficient evidence to state with confidence that the hyper kinetic circulation of pregnancy begins to develop during the *second month* is well established by the end of the third month, increases slightly and gradually to the thirty second week and thereafter declines Much of this evidence has been summarised by Morgan Jones (1951)

Clinically the palms flush the extremities are hot the digital vessels throb capillary pulsation may be demonstrated the pulse is full and bounding the heart rate quickens the venous pressure rises the soft tissues become more tense and there may be slight œdema The heart itself is hyperdynamic the cardiac impulse is forcible and displaced slightly to the left aortic and pulmonary systolic murmurs heard at apex and base advertise the increased blood flow a loud third sound confirms rapid ventricular filling and X rays may reveal slight diastolic enlargement Ectopic beats are common The electrocardiogram often shows a prominent S wave in lead I and a conspicuous Q wave and inverted T wave in lead III (fig 21 04) *due to rotation of the heart*

Special tests reveal the following

(1) Oxygen consumption is increased by 15 to 20 per cent (Burwell 1937 1938)

(2) The cardiac output increases by 50 per cent (Palmer and Walker 1949 Hamilton 1949)

(3) Retention of sodium and water results in considerable hæmodilution *the increase of plasma volume reaching a maximum of 45 per cent above normal by the thirty second week* (Cohen and Thomson 1936 Thomson *et al* 1938) after which diuresis sets in (Chesley 1943)

(4) The general venous pressure rises as a result of the increased blood volume sometimes considerably the venous *pressure in the legs* is particularly high owing to the local obstructing effect of the enlarged uterus (Burwell *et al* 1938) Compression of the inferior vena cava is common in the supine position and the fall in right atrial pressure and cardiac output that may result from pooling of blood in the legs may cause faint ness and seriously interfere with physiological studies

The circulatory effects of pregnancy are attributed chiefly to the in

creased blood volume whilst the rise in oxygen consumption and a uterine arterio venous shunt (Burwell 1938) are contributory

Whilst the normal heart tolerates the added load easily enough diseased hearts may not When trouble occurs it usually *begins* early often by the end of the third month The *onset* of heart failure proper occurs with increasing frequency up to the end of the thirty second week after which it steadily declines (Hamilton and Thomson 1942)

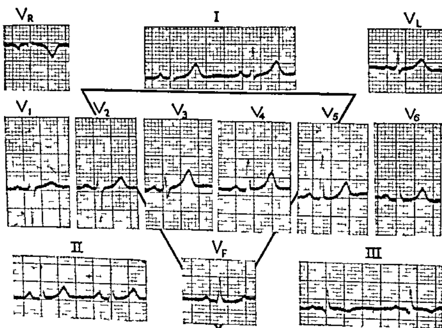


Fig 21 04—Electrocardiogram showing characteristic appearances associated with pregnancy

Frequency and types of heart disease associated with pregnancy

Heart disease was recognised in 1 3 per cent of 80 422 pregnant women analysed by Haig and Gilchrist (1949) Of their 1 100 heart cases 94 per cent were rheumatic 3 6 per cent congenital 1 8 per cent hypertensive and 0 6 per cent miscellaneous Similar figures (see table) have been published by Hamilton (1935) Morgan Jones (1951) and many others

Hypertension associated with toxæmia of pregnancy is obviously excluded from these statistics since this occurs in 5 per cent of all pregnancies Toxæmia is particularly dangerous in cases of heart disease not because of the hypertension (except in relatively rare cases of hypertensive heart disease) but because of the sodium and water retention

The mortality from heart disease in pregnancy averages 4 5 per cent (Jensen 1938 Jones 1951) but naturally varies greatly according to the

NO OF PREGNANT WOMEN WITH HEART DISEASE	NATURE OF HEART DISEASE (frequency per cent)				AUTHORS
	RHEUMATIC	CONGENITAL	HYPER TENSIVE	MISC	
1 335	93	5 2	—	1 8	Hamilton (1935)
1 100	94	3 6	1 8	0 6	Haig and Gilchrist (1949)
485	90	6 8	1	1 1	Morgan Jones (1951)

severity of the lesion If patients are classified according to their grade of previous effort intolerance as defined on page 521 then the mortality from heart disease increases from about 0 4 per cent in grades 0 to 2A 5 3 per cent in grade 2B and 22 6 per cent in grades 3 and 4 (Jensen 1938) These figures were based on 1,428 cases collected from the literature over 90 per cent of them rheumatic Hamilton (1947) reported somewhat similar figures in a series of 1 335 cases of heart disease in pregnancy (93 per cent rheumatic) the mortality in grades 0 to 2A was 2 per cent as it was in non pregnant controls with heart disease of similar degree whereas in grades 2B to 4 the mortality was 18 per cent, compared with 6 7 per cent in non pregnant controls When there was atrial fibrillation the maternal mortality was 32 per cent (8 per cent in non pregnant controls)

Infant mortality should also be considered In Hamilton s series this was 8 6 per cent in the favourable group 31 per cent in the unfavourable group and 50 per cent when there was atrial fibrillation

Figure 21 05 which has been constructed from data published by Jensen (1938) shows that mortality increases steadily throughout pregnancy and reaches its climax during labour itself and the ensuing 24 hours

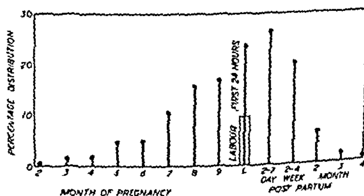


Fig 21 05—Chart showing when death occurs in fatal cases of heart disease associated with pregnancy

nearly 24 per cent of the 462 deaths analysed occurring at this time but the puerperium is also dangerous 26 per cent of the deaths occurring between the second and seventh day after delivery and 20 per cent during the next fortnight Werko (1954) regards the first 48 hours after delivery as the most dangerous period

The commonest causes of death are congestive heart failure (36 per cent) and pulmonary œdema (27 5 per cent) (Jensen 1938) The latter is chiefly responsible for death during pregnancy, the former for death during or after delivery (Morgan Jones 1951)

General Management

Irrespective of the type of heart disease present the following general rules are widely accepted

1 Patients with grade 0 to 1 effort intolerance should not ordinarily be dissuaded from having a family and should experience little extra trouble during pregnancy and the puerperium

2 Patients with grade 2B to 4 effort intolerance who cannot be radically improved by present methods of treatment should be advised not to have a family and pregnancy should be terminated within the first three months if already present If the nature of the cardiac lesion is beyond foreseeable therapeutic developments sterilisation should also be carried out but not otherwise If the pregnancy is already advanced it is usually best to allow it to continue to its natural conclusion

3 Patients with grade 2A effort intolerance should be considered individually and social factors may be taken into account

4 If the cardiac lesion calls for surgical treatment the operation is best undertaken before pregnancy if the patient is already pregnant the operation should be carried out without delay if effort intolerance is grade 2B or more or deferred for a year or so if effort intolerance is grade 0 to 2A The pregnancy itself should not be terminated and sterilisation is unjustified

5 The best means of combating the adverse effect of pregnancy on the cardiovascular system is the low sodium diet supported if necessary by mercurial diuretics mictine diamox or resins Digitalis is not indicated when pulmonary œdema is due to mitral stenosis but is helpful in cases of atrial fibrillation and congestive heart failure Prolonged rest preferably in bed should be enforced until the situation is well in control

RHEUMATIC HEART DISEASE AND PREGNANCY

There are some who maintain that any woman who has rheumatic heart disease should be advised against having any children They argue that pregnancy affects her adversely and that the strain of bringing up children shortens her life Others feel that to forfeit so much human happiness on these grounds is both undesirable and unnecessary Is life so precious to

prolong if so much of its meaning is taken away? Moreover available statistics barely support the first argument Thus in four combined series collected by Jensen (1938) the average age of death in spinsters or nulliparous women with mitral stenosis was 36 6 in married women with families it was 40 3 Again, Bunim and Rubricius (1948) could find no significant difference in the life histories of 169 rheumatic mothers and 215 rheumatic childless women Of course, the childless women may have been advised against pregnancy owing to the severity of their condition so that the two groups may not be strictly comparable there is insufficient evidence on this point It is certain however that many women with mitral stenosis unaware that there is anything wrong with them have large families and lead normal lives until the lesion is discovered in later life

Over 90 per cent of all cases of heart disease associated with pregnancy are rheumatic and at least four fifths of these have mitral valve disease usually stenosis The increased blood volume and raised cardiac output result in further elevation of the left atrial pressure and since the rapidity of the change leaves little time for the development of physiologically protective mechanisms hæmoptysis and acute pulmonary œdema are relatively common Less frequently and chiefly in those with a high pulmonary vascular resistance uncontrolled atrial fibrillation myocardial fibrosis or active rheumatic carditis the extra load results in congestive heart failure Pulmonary embolism increases the mortality during the puerperium

The majority of patients with uncomplicated mitral stenosis who experience serious trouble during pregnancy *begin to develop symptoms of* increasing pulmonary congestion towards the end of the third month conversely if all is well at the end of the first trimester without prophylactic treatment little trouble is likely to arise later Clinically when assessing the physiological situation due allowance must be made for the fact that 60 per cent of normal women experience breathlessness during pregnancy (Hamilton and Thomson 1942) and that a slight rise of venous pressure is normal

When considering the question of future pregnancy in cases of rheumatic heart disease it is vitally *important to make sure* whether surgical treatment is possible or not In cases of *aortic or mitral incompetence* for example pregnancy should be avoided or terminated within the first few months if effort intolerance is grade 2A or more for these lesions cannot yet be corrected surgically and any deterioration may well prove disastrous moreover both aortic and mitral incompetence must be advanced before grade 2 effort intolerance develops

Cases of mitral stenosis on the other hand are relatively safe if symptoms are already moderate or severe, valvotomy should be carried out before pregnancy if effort intolerance is only grade 1 to 2A and the pulmonary vascular resistance normal valvotomy should *be deferred and pregnancy* allowed to take its natural course if serious symptoms then develop

valvotomy may be performed during pregnancy which need not be terminated Cases of mitral stenosis with a raised pulmonary vascular resistance require valvotomy before pregnancy irrespective of the grade of effort intolerance for they are likely to develop congestive heart failure late in pregnancy or during the puerperium with or without pulmonary embolism When the patient is already pregnant valvotomy should be performed as soon as possible and if the operation is technically successful the pregnancy should be allowed to continue

Although *rheumatic aortic stenosis* may be relieved surgically the high mortality and relatively indifferent results of the present operation are not reassuring and patients with this lesion should be managed in respect of pregnancy like patients with aortic incompetence

Previous statistics showing no difference in the mortality rate from mitral stenosis and the other valve lesions in relation to pregnancy do not apply now that mitral stenosis can be relieved surgically

Normal pregnancy is safe after technically successful valvotomy in cases with previous mitral stenosis but toxæmia can be very dangerous when there is mild residual stenosis pulmonary œdema then occurring very readily One of the writer s post operative cases died under just these circumstances and necropsy revealed a partially split valve with an orifice measuring approximately 2 5 × 1 cm

Retention of sodium and water must be countered strenuously with a rigid low sodium regime

Cases of active rheumatic carditis are probably best terminated as soon as the state of the heart permits for there is no knowing what the sub sequent course will be and a relapse later in pregnancy may prove very serious

When pregnancy is not advised prevention is best insured by a simple sterilising operation Termination of pregnancy is by therapeutic abortion in the first three months by abdominal hysterotomy from the fourth to the sixth month by induced labour or by Cæsarean section during the seventh and eighth months by natural means or by Cæsarean section at term The choice must rest with the obstetrician

CONGENITAL HEART DISEASE

Any form of congenital heart disease compatible with adult life may obviously be associated with pregnancy *In practice* the more common lesions include atrial septal defect patent ductus arteriosus pulmonary stenosis with normal aortic root coarctation of the aorta ventricular septal defect and Fallot s tetralogy—in that order of frequency With the exception of ventricular septal defect all these lesions can now be repaired or relieved surgically and if severe enough to warrant such treatment the operation should be carried out before pregnancy If the patient is already pregnant surgical treatment should not be delayed and the pregnancy need not then be terminated Patients who have had severe congenital heart

disease cured repaired or sufficiently relieved surgically may have one or more babies subsequently without ill effect Mild congenital lesions are no bar to pregnancy and do not adversely influence obstetrical mortality

Atrial septal defect of mild or moderate degree is compatible with many normal pregnancies If severe however it should be repaired with the aid of hypothermia, preferably before, but if necessary during the early months of pregnancy

Patent ductus arteriosus is now treated surgically as a routine however mild If a small duct is discovered for the first time during pregnancy it is better to defer operative treatment but ducts of moderate or large size are better ligated without delay

Severe pulmonary stenosis has been relieved during pregnancy on several occasions and patients operated on previously have had normal pregnancies subsequently The second statement also applies to cases of Fallot's tetralogy who have been successfully relieved by pulmonary valvotomy or infundibular resection

Coarctation of the aorta may be discovered for the first time during pregnancy on account of the hypertension Although the majority of cases go through to term safely a few end disastrously with rupture of the aorta and to avoid this risk surgical repair is probably best undertaken at once if the condition is diagnosed within the first three months If not recognised until later however it may be better to defer the operation and to allow the pregnancy to proceed delivering the baby by means of Caesarian section to avoid the risk of vascular accidents during labour (Benham 1949)

Since *ventricular septal defect* cannot yet be repaired satisfactorily severe cases should avoid pregnancy or should have the pregnancy terminated in the early months Cases of mild or moderate severity run no special risk Sterilisation is not justified because successful surgical repair may soon be possible

BACTERIAL ENDOCARDITIS

Before the introduction of penicillin the life of the fœtus was the main consideration The situation is now reversed however and every effort should be made to save the mother As heart failure is now the chief cause of death from bacterial endocarditis, termination of pregnancy may often be desirable

THYROTOXICOSIS

One of the few known factors that may aggravate or precipitate thyrotoxicosis is pregnancy It follows that thyrotoxic women should be advised against pregnancy until they are cured Improvement on rest and iodine or as a result of thiouracil treatment is not enough such cases tend to relapse during pregnancy At least a year should pass after partial thyroidectomy or thiouracil cure before conception should be considered

If a woman is thyrotoxic and already pregnant therapeutic abortion should be considered during the first three months if not seen until gestation is more advanced it may be wiser to take the patient to term with the aid of thiouracil Subtotal thyroidectomy is better deferred owing to the risk of relapse The dose of thiouracil must be the minimum that is effective for there is some danger of its causing goitre in the fœtus the simultaneous administration of small doses of iodine or thyroid may prevent this

HYPERTENSION

High blood pressure discovered during pregnancy may be due to chronic persistent hypertension (usually essential) or to toxæmia of pregnancy Essential hypertension may be aggravated by pregnancy but with rest diet and sedatives mild cases can be taken to term Nevertheless women with high basal blood pressures (above 160/100 mm Hg) should be advised against pregnancy in view of the increased risk of toxæmia the high infant mortality (66 per cent according to Browne 1947) and the chances of serious aggravation For similar reasons pregnancy should be terminated in women with relatively high pressures in the first three months Hypertension associated with toxæmia of pregnancy is a separate problem and will not be considered here

ARTERIO VENOUS FISTULA

Arterio venous fistula may be congenital (circoid aneurysm) or acquired (usually as a result of a perforating wound) and may occur in any situation particularly in the brain limbs or lung

Physiology

Experimentally an artificial arterio venous fistula between the femoral artery and vein for example results in an immediate fall of blood pressure slight elevation of the venous pressure acceleration of the pulse and rise of cardiac output whilst locally the distal part of the leg becomes œdematous the skin cold and the toes occasionally gangrenous (Holman 1937) Physiologically the fistula acts as a zone of low resistance in the arterial circulation The drop in blood pressure is due to the fall in total peripheral resistance the greatly increased blood flow through the fistula tends to raise the venous pressure the tachycardia is due to the fall in blood pressure acting on carotid and aortic baroreceptors the rise in venous pressure usually being too slight to stimulate the Bainbridge reflex the increased cardiac output is due to a combination of the fall in total peripheral resistance which encourages the heart to empty itself more completely the slight rise of venous filling pressure and the tachycardia Locally œdema of the leg has been attributed to great elevation of the femoral venous pressure coldness pallor and gangrene to a diminished blood flow distal to the lesion for it is much easier for blood to pass through the fistula than through the normal channels (Holman 1937)

After a variable time several important changes take place The blood volume increases and raises the venous pressure more conspicuously the cardiac output is thus augmented and the blood pressure gradually restored The shunt through the fistula is increased by these changes but sooner or later a state of balance is reached Locally, the vessels carrying the shunt become dilated even aneurysmal the artery below the fistula is affected as well as that above, because blood entering the distal part of the terminal artery from collateral channels is forced backwards by the peripheral resistance to the fistulous zone of lower resistance The dilated arteries that accommodate the increased flow become thin walled and the veins receiving the flow at a higher pressure than that to which they are accustomed become arterialised in other words both become anatomically adjusted to the new pressure With the increased blood volume and total cardiac output the blood flow to the distal part of the leg is not only restored but often becomes greater than normal The leg becomes hot and the veins distended and when initial œdema has subsided the leg usually remains larger than its fellow (Holman 1937)

The physiology of congenital and acquired arteriovenous fistula is the same as that found experimentally both in the initial and later stages of development Local effects were well described by Reid (1925) amongst others and Cohen *et al* (1948) confirmed that the blood flow in the affected limb distal to the fistula was diminished in early cases and increased in cases of long duration The increased blood volume was demonstrated by Rowntree and Brown (1929) and the raised cardiac output by Warren *et al* (1947) and Cohen *et al* (1948) In congenital cases the increased vascularity of ununited epiphyses in the affected limb may lead to considerable hypertrophy of one arm or leg (Horton 1932)

CONGENITAL CIRCOID ANEURYSM

Circoid aneurysm consists of a twisted mass of dilated vessels in which artery and vein are in direct communication One or more superficial hæmangiomas may be seen elsewhere or there may be a family history of such nævi

The cerebral type may give rise to epilepsy subarachnoid hæmorrhage or ophthalmoplegic migraine Examination may reveal a systolic murmur heard best through the eye ball on the affected side or sometimes over the skull The diagnosis may be proved by finding an unduly high oxygen saturation in samples of blood obtained from the ipsilateral jugular vein The lesion may be localised by means of angiography 10 to 20 ml of 70 per cent diodone or other radio opaque substance being injected rapidly into the carotid artery and skiagrams of the cerebral vessels being obtained at the appropriate moment The condition should be distinguished from berry aneurysm and from Sturge s disease *in* which facial and pial nævi without arterio venous communications are associated with calcification of brain substance epilepsy mental retardation and glaucoma (Nussey) and



Fig 21 06 (a)—Skiagram showing a congenital arterio venous aneurysm of the lung The appearances bear some resemblance to those of pulmonary tuberculosis
(b) Angiocardiogram showing diodone filling the aneurysm

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Miller 1939) Treatment consists of ligation of the common carotid artery on the side of the lesion if after trial compression hemiplegia or other serious ischæmic symptoms do not occur The risk of such an untoward event increases progressively with the age of the patient

Circoid aneurysm in a limb presents similar features to those of its traumatic cousin It may be situated anywhere from the shoulder or pelvic girdle to the hand or foot There is usually an increase in blood flow to the limb which may be longer and larger than its fellow Occasionally however there is ischæmic atrophy in one or more digits distal to an aneurysm in the hand or foot The veins stand out are sometimes varicose and may exhibit arterial pulsation and the skin temperature is raised It may be possible to locate the aneurysm with precision by observing the effect on the local and general circulation of compressing the various arteries of the limb at appropriate points An impressive machinery murmur and thrill may be appreciated over the fistula itself Venous blood from the affected limb may be more saturated with oxygen than venous blood from the unaffected limb The exact location and construction of the aneurysm may be demonstrated by means of angiography Treatment is more difficult than in traumatic cases Excision is usually impossible owing to the diffuse nature of the lesion moreover affected vessels are physiologically abnormal and fail to constrict when injured so that severe and

prolonged hæmorrhage may follow surgical interference Ligation of the main vessels leading to the aneurysm (above and below) may be possible but deep X-ray therapy is usually best

Congenital arterio venous aneurysm in the lung, which is associated with telangiectasis elsewhere in 50 per cent of cases (Baer *et al* 1950), causes venous blood from the pulmonary artery to be shunted directly into the pulmonary veins and thence into the arterial circulation, at the same time the blood flow through the rest of the lung may be reduced the steep pressure gradient through the aneurysm offering the easier pathway The result is a lowered arterial oxygen saturation in the region of 70 to 75 per cent (Burchell and Clagett 1947) central cyanosis polycythæmia and clubbing Most of the cases reported have been in children or young adults Hæmoptysis has occurred in 50 per cent The heart itself is normal but there may be a continuous machinery murmur over the affected part of the lung A skiagram may show a rounded or irregular opacity (fig 21 06a) which on fluoroscopy may be seen to pulsate tomograms may reveal a dilated artery and vein in close relationship to the abnormal shadow and angiocardiograms may show the abnormal vessels filled with diodone (fig 21 06b) (Baker and Trounce 1949) Lesions may be single or multiple unilateral or bilateral Calcification may occur in the wall of an aneurysm (fig 21 07) One case (a girl aged 9) seen by the author died with cerebral abscess The condition should be distinguished from patent ductus arteriosus helping to correct pulmonary or tricuspid atresia Treatment by lobectomy or pneumonectomy is curative unless there are several widely distributed aneurysms (Barnes *et al* 1948)

Fig 21 07—Calcification in the wall of an arterio-venous aneurysm
Ack owl dgment t D Ch l B k

Congenital coronary arteriovenous fistula is very rare but is mentioned in view of its peculiar interest to cardiologists Details of a few cases that have been reported including a new one of my own are given in the accompanying table It will be noticed that four were symptom free and were detected only because of the continuous thrill and murmur When this was maximum in the third left space the fistula was between the left circumflex coronary artery and the coronary sinus when it was maximum low down

AUTHOR	AGE	SEX	SYMPTOMS	SITE OF A V MURMUR OR THRILL	E C G	X RAY	CORONARY ARTERY INVOLVED	DIAGNOSIS
Halpert (1930)	54	M	Nil	—	—	—	Right	P M
Paul *et al* (1949)	9	M	Nil	Right sternal edge 4th and 5th space	Normal	Normal	Right	Clinical and operative
Cross (quoted by Paul *et al*)	16	M	Nil	3rd and 4th left spaces	—	—	? left circumflex	Operation
Davison *et al* (1955)	58	F	Congestive heart failure	2nd 3rd 4th left spaces	A fib QRS balanced	General enlargement congested lungs	Left circumflex	P M
Wood	60	M	Nil	4th and 5th spaces right sternal edge	Normal	Calcified A V aneurysm	Right	Clinical X ray

the right sternal edge the fistula was between the right coronary artery and the coronary sinus Cardiac catheterisation was carried out in only one instance and a left to right shunt at atrial level was demonstrated the pulmonary blood flow was 6 9 litres per minute the systemic 3 1 (Davison *et al* 1955) The diagnosis could have been made had samples from the coronary sinus been obtained In my own case the diagnosis was obvious clinically and radiologically (fig 21 08) and catheterisation was not justified Of these five cases this was the only one with calcification



(a) Right anterior oblique view



(b) Left anterior oblique view

Fig 21 08—Calcified arterio venous fistula between the right coronary artery and coronary sinus

ACQUIRED ARTERIO VENOUS ANEURYSM

The *great majority of acquired arterio venous aneurysms* are due to perforating gunshot wounds in war and are seen most often in connexion with the femoral brachial or carotid arteries Occasionally they may be syphilitic mycotic or artificial Arterio venous shunting may also occur in highly vascular structures such as the thyroid gland in severe thyrotoxicosis or as a result of overdosage with thiouracil (page 879) the uterus in pregnancy (page 903) and the bones in active Paget s disease (page 917)

The local signs and the effect on the general circulation are *similar* to those in experimental arteriovenous fistula At first the affected limb swells the skin becomes cold and there is danger of peripheral gangrene When a state of balance is reached and compensatory adjustments have been made the œdema subsides and the limb becomes warmer than its fellow The

veins distend and may pulsate A coarse machinery murmur and thrill are invariable over the lesion itself

The general circulation is hyperkinetic and if the shunt is large enough paroxysmal cardiac dyspnœa or signs of congestive heart failure may develop as observed by Reid (1920) If the shunt is temporarily obliterated by digital compression of the femoral artery just above the lesion, the pulse rate falls 10 to 30 beats per minute (Branham's sign) the blood pressure rises 10 to 15 mm Hg the venous pressure falls slightly and the cardiac output falls (Stead and Warren, 1945) but capillary pulsation is accentuated (Lewis and Drury 1923) Slowing of the pulse is due to the rise in blood pressure and is abolished by atropine (Kramer and Kahn 1946)

Cardiac enlargement is almost certainly due to the raised cardiac output and increased stroke volume The hyperkinetic circulation is maintained by tachycardia and raised venous filling pressure whilst the peripheral resistance is further reduced by vasodilatation in skin and muscle

Treatment Any arterio venous aneurysm large enough to influence the general circulation should be repaired Smaller lesions may be left alone if causing no local symptoms and some of them become obliterated spontaneously Every effort should be made to repair the artery by lateral suture or graft so that the normal circulation is preserved (Junghann 1943) Ligation of artery and vein above and below the aneurysm is less satisfactory the resulting circulation through the brain or limb being sometimes inadequate Simple ligation of the artery above the fistula was condemned as long ago as 1886 by Bramman for this frequently results in peripheral gangrene

THE HEART AND CIRCULATION IN BERI BERI

In modern civilised communities pure beri beri is rare the clinical picture being commonly influenced by deficiencies in vitamins other than aneurin (B_1) and by associated conditions especially chronic alcoholism Aneurin (thiamine) in association with other components of the vitamin B complex is found chiefly in unpolished rice marmite liver yeast wheat and other grains It is used by the body in carbohydrate metabolism its chief known function being concerned with the oxidation of pyruvic acid which is formed from lactate When there is insufficient aneurin carbohydrate metabolism is held up at this point and an excess of pyruvic acid accumulates in the blood (Peters 1939) It follows that any condition in which carbohydrate metabolism is excessive predisposes to beri beri in that aneurin requirements are heavier When in addition the vitamin B intake is reduced at the same time as in chronic alcoholism vomiting of pregnancy and thyrotoxic crises beri beri may well develop

The normal requirement of aneurin is about 1 mg daily for an adult and is supplied adequately by the ordinary European diet Special ulcer diets however unless supplemented may be deficient and psychoneurotic—

patients with severe anorexia and vomiting may not receive a sufficient supply of the vitamin Beri beri was common in German concentration camps and Japanese prison camps during the second world war, although usually complicated by other vitamin deficiencies, and has always been relatively common in the Far East when the basic food has been polished rice

Aneurin deficiency is rarely gross in civilised communities and so the presence of some additional factor is commonly needed before the effects of slight deficiencies are brought to light Under these conditions beri beri is atypical for such patients are apt to be middle aged or elderly and the classical signs may be masked by hypertension coronary sclerosis or emphysema in these mixed cases no clear picture of beri beri develops (Konstam and Sinclair 1940)

Behaviour of the heart and circulation The pure disease was studied in Java by Wenckebach (1928 1934) The essential features included a hyper kinetic circulation vasodilatation enlargement of the heart and dilatation of the pulmonary artery Few accurate cardiac output studies have been carried out but the clinical description and the swift circulation time (Weiss and Wilkins 1936–37) leave little doubt that it is high Heart failure may develop suddenly and fulminating cases occur in which death results within 24 to 48 hours of alleged onset of symptoms (Hashimoto 1937) Even in Great Britain cases have been described in which heart failure has occurred remarkably suddenly and unexpectedly leading to a rapidly fatal issue (Wood 1939)

The cause of the hyperkinetic circulation is vasodilatation The drop in peripheral resistance encourages the heart to empty itself more completely whilst the fall in blood pressure causes reflex tachycardia As in all hyper kinetic circulatory states associated with a lowered peripheral vascular resistance (except chronic anæmia) retention of sodium and water by the kidneys increases the blood volume raises the venous pressure and so further increases the cardiac output The remarkable quietening of the circulation that follows the injection of 1 ml of pitressin and the stormy reaction to 1 mg of subcutaneous adrenaline (Wenckebach 1928) confirm the important role of vasodilatation The sudden rise in pulse rate and cardiac output that follow the subcutaneous injection of 10 mg of mecholin or the inhalation of amyl nitrite demonstrate clearly the effect of vaso dilatation on the circulatory hæmodynamics in normal subjects

The heart itself shows little specific at necropsy, the disturbance being biochemical not structural

Diagnosis The clinical diagnosis of cardiovascular beri beri rests on an appropriate dietetic history the demonstration of a hyperkinetic circula tion radiological appearances showing conspicuous dilatation of the pul monary artery associated with overaction and general enlargement of the heart the response to pitressin and adrenaline associated polyneuritis and on the finding of a raised blood pyruvic acid or reduced amounts of

aneurin in blood (Jansen 1938 Sinclair 1938) or urine (Harris *et al* 1938 McAlpine and Hills 1941)

Peripheral neuritis usually begins with pain in the calves on walking similar in character to intermittent claudication Associated weakness of the legs marked tenderness of the calves numbness and tingling of the fingers and toes loss of deep tendon jerks and glove and stocking anæsthesia are usually found

Evidence of deficiencies in other vitamins especially of the vitamin B group is helpful in proving inadequacy of the diet

Treatment It must be stressed that the symptoms of beri beri may begin abruptly and that the course of the disease may be fulminating death occurring within a few days of the onset Once the diagnosis has been made there may be no time to lose Again the possibility of vitamin B_1 deficiency should always be borne in mind in any case of heart failure of obscure origin Here is one of the fatal forms of heart disease which is curable

The patient should be put to bed immediately and aneurine hydrochloride should be given at once intravenously in an initial dose of 50 to 100 mg The effect is dramatic if not given too late Subsequent doses should be of the order of 10 to 20 mg per day for a fortnight orally or parenterally and followed by an adequate diet An abundance of the other components of the vitamin B group is also advised

Fulminating cases should benefit by repeated injections of pitressin (1 ml 4 hourly) until the vitamin has had time to work but care must be taken to avoid hydræmia by keeping the salt and water intake as low as possible

Chronic alcoholics cases of severe thyrotoxicosis Simmond s disease or anorexic nervosa and women vomiting in pregnancy should be given 2 to 5 mg of aneurin daily as a precautionary measure

PAGET S DISEASE OF BONE

The hyperkinetic circulation associated with extensive active Paget s disease was first clearly demonstrated by Edholm Howarth and McMichael in 1945 The general cardiovascular findings closely simulate those associated with arterio venous aneurysm In the case described by Edholm *et al* the blood flow through actively diseased bones was estimated to be 3 to 4 litres per minute and the total cardiac output was 13 litres per minute The venous pressure was elevated and there was dependent œdema Further observations on other cases of active Paget s disease have shown that the heart is not usually overloaded for it is capable of increasing its output by means of tachycardia or a greater rise of venous filling pressure on the other hand paroxysmal cardiac dyspnœa may then occur (McMichael 1947)

Paget s disease also encourages metastatic calcification especially Monckeberg s sclerosis and calcification of the valve rings of the heart

Extension to the interventricular septum may involve the bundle of His or its branches with the production of complete heart block or bundle branch block respectively (*Harrison and Lennox, 1948*)

Cor pulmonale secondary to thoracic deformity from Paget s disease has also been described (Wilks 1869)

Diagnosis If aortic incompetence and valve calcification are both present the clinical diagnosis of Paget s disease may be overlooked in favour of atherosclerotic aortic valve disease As long as the condition is borne in mind however diagnosis is easy for skiagrams of the bones show charac teristic changes and the blood alkaline phosphatase is very high

HEPATIC FAILURE

It has become increasingly evident that advanced disease of the liver may lead to a hyperkinetic circulatory state in addition to the well known palmar flush and cutaneous spider nævi The usual cause is secondary carcinoma but common cirrhosis and even serious infective hepatitis may be responsible It appears that the liver normally detoxicates some vaso depressor substance and that this substance accumulates when the organ is failing (Shorr *et al* 1945) vasodilatation results in the same chain of physiological adjustments that have been described in arteriovenous fistula and beri beri The remarkable effect of hepatic failure on the circulation may be seen sometimes in advanced cases of heart failure when vaso dilatation replaces peripheral vasoconstriction

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CHAPTER XXII

TRAUMATIC LESIONS OF THE HEART AND GREAT VESSELS

SPONTANEOUS LESIONS

SPONTANEOUS traumatic lesions of the heart or great vessels include dissecting aneurysm of the aorta rupture of a hypoplasic aorta or syphilitic aortic aneurysm ruptured valve cusps in bacterial endocarditis rupture of a congenital syphilitic or mycotic aneurysm of a sinus of Valsalva into the right side of the heart rupture of chordæ tendineæ in rheumatic or bacterial endocarditis, and rupture or perforation of the heart or ventricular septum secondary to cardiac infarction or ventricular aneurysm The majority of such lesions have been described elsewhere *as complications of the diseases mentioned* Only *dissecting* aneurysm and rupture of an aneurysm of a sinus of Valsalva into the right side of the heart remain to be considered here

DISSECTING ANEURYSM

Definition

Dissecting aneurysm was so called by Lænnec (1826) and means dissection of the media of the aorta by extravasated blood that has penetrated between its coats from the vasa vasorum or from the lumen of the vessel

Incidence

About 1 per cent of all sudden deaths are due to dissecting aneurysm (Mote and Carr 1942) Hospital records which include relatively few such deaths give an approximate incidence of one dissecting aneurysm in every 450 necropsies The Registrar General s figures for 1953 show it to be responsible for about 0 5 per cent of all cardiac deaths in England and Wales Men are more susceptible than women in the ratio of 2 5 1 (Levinson *et al* 1950) Patients are commonly between 50 and 60 years old but 24 per cent are under 40 (Schnikter and Bayer 1944) and cases have been recorded in children (e g Galbraith Gardner and Hardwick 1939) About 50 per cent of dissecting aneurysms in women have occurred during pregnancy (Schnikter and Bayer 1944)

Etiology and pathology

Virchow s original conception that dissection follows an intimal tear at the site of an atheromatous ulcer is no longer tenable for a tear at such a site is now known to be rare (Shennan 1934) Although hypertension and atheroma are usually associated they are not essential the intima may be normal and not even ruptured (Tyson 1931)

Dissection is always within the media commonly begins in the ascending aorta and appears to be closely related to cystic medial necrosis (Erdheim 1929) The cause of such necrosis is unknown Tyson s thesis that it was due to obliterative endarteritis of the vasa vasorum has not been con firmed Cystic necrosis without dissection may be found sometimes in routine necropsies (Moritz, 1932 Rottino 1939) Whether hæmorrhage into the diseased media commonly follows an intimal tear, or whether it comes from the vasa vasorum (the intimal tear then being due to secon dary rupture) remains uncertain When the intima is intact hæmorrhage obviously cannot come from the lumen of the aorta On the other hand intimal tears may undoubtedly be primary for they may occur in healthy ascending aortas without subsequent dissection (Peery 1942) Occasionally hæmorrhage occurs into an area of cystic necrosis of the media without dissection the hæmatoma then becoming organised and causing no trouble (Shennan 1934)

It has recently been suggested that cystic medial necrosis and dissecting aneurysm may be due to defective formation or excessive destruction of chondroitin sulphate the chief mucopolysaccharide of the ground sub stance of the aorta (Ponseti and Baird 1952) These authors noted the high frequency of dissecting aneurysm and kyphoscoliosis in growing rats fed on 50 per cent sweet pea meal the toxic agent being β aminoproprionitrile The fault in the ground substance that results from this agent is believed to be responsible for both skeletal and aortic flaws Bean and Ponseti (1955) found that seven out of 27 clinical cases of dissecting aneurysm had gross kyphoscoliosis

Dissection not infrequently complicates congenital hypoplasia of the aorta usually part of Marfan s syndrome an inherited mesodermal dyscrasia which may well incorporate faulty ground substance A similar flaw may explain the frequency of aortic rupture or dissection in cases of coarctation of the aorta

Dissection may spread proximally and involve the root of the aorta causing aortic incompetence occasionally the coronary arteries are dis sected and occluded Dissection usually spreads distally however may travel the whole length of the aorta and may proceed along any of its branches Ischæmic effects from occluded visceral or parietal vessels are common The majority of cases die from external rupture usually into the pericardium (Strassmann 1947) sometimes into the left pleural cavity or elsewhere Occasionally dissection associated with an intimal tear in the ascending aorta ruptures back into the lumen of the vessel at some distal point forming an alternative or double aortic channel (double barrelled aorta) This is found in the majority of cases that recover (Shennan 1934)

Clinical features

Dissection of the aorta may be precipitated by effort (Gager 1928) but is more often spontaneous A typical attack begins suddenly with severe

pain in the centre of the chest or in the præcordial area The pain may be gripping tearing shooting, or vice like and usually lasts for hours it may radiate to the head and neck to the back—less often to the arms Later in the attack it may spread to the lumbar regions or abdomen and occasionally to the legs depending on the extent of the dissection In perhaps half the cases however pain is slight or absent (Baer and Goldburgh 1948)

Breathlessness is nearly as common as pain (Hamburger and Ferris 1938) and syncope occurs in about 10 per cent of cases (Levinson *et al* 1950) Attacks may therefore closely resemble coronary thrombosis but in cases that survive the blood pressure usually remains high and the electrocardiogram normal moreover, dilatation of the aorta may often be seen in skiagrams (fig 22 01) (Wood, Pendergrass and Ostrum 1932) Fever and leucocytosis are the rule not the exception (Baer and Goldburgh 1948)

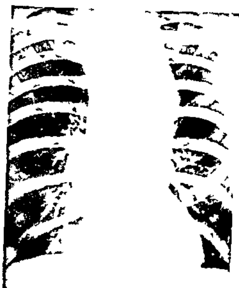


Fig 22 01 —Dissecting aneurysm of the aorta

Other findings depend upon the site and extent of the dissection upon which branches of the aorta are occluded and upon the site of external rupture Aortic incompetence may develop when the root of the aorta is dissected (Weiss 1935) and is being noted with increasing frequency (David *et al* 1947) myocardial infarction may occur if the left or right coronary artery is occluded giving rise to the appropriate electrocardiographic pattern (Wainwright 1944) Pericardial friction is heard occasionally and hæmopericardium may be recognised before death

Dissection of major arteries leads either to occlusion of the vessel or to increased amplitude of pulsation due to spontaneous periarterial sympathectomy (Weisman and Adams 1944) Occlusion of one or other of both carotid arteries may cause hemiplegia mental confusion or coma of the anterior spinal artery, paraplegia of arteries to the limbs loss of the peripheral pulse and perhaps ischæmic pain of the renal artery, hæmaturia —and so on Occasionally a pulse that has been absent may re appear a a result of rupture re entry (Lawrence 1935) A systolic murmur and thrill may develop over partly occluded vessels including the aorta (McGeachy and Paullin 1937) Left hæmothorax is found in about 12 per cent of cases (Baer and Goldburgh 1948) Hæmorrhage into the mediastinum may be responsible for cough and dysphagia An abdominal mass may become

palpable Hæmoptysis hæmatemesis and hæmaturia occur occasionally

Cases that survive the original dissection may present themselves later with congestive heart failure associated with aortic incompetence When there has been no history of pain such cases have usually been diagnosed erroneously as syphilitic aortic incompetence despite negative Wassermann reactions (Gouley and Anderson 1940 Flaxman 1942)

Angiocardiography may help to prove the diagnosis (Golden and Weens 1949) but is not advised in the acute or subacute stage

Prognosis

According to Shennan (1934) about 10 per cent of all cases of dissecting aneurysm recover from the attack usually owing to rupture re entry The majority succumb later to heart failure either as a result of aortic incompetence or from associated hypertensive heart disease

Treatment

No treatment is likely to influence the course of dissection Morphine should be given freely to combat pain If the patient survives the initial attack he should be kept in bed for at least a month

RUPTURE OF AN ANEURYSM OF AN AORTIC SINUS (SINUS OF VALSALVA) INTO THE RIGHT ATRIUM RIGHT VENTRICLE OR PULMONARY ARTERY

Aneurysm of one of the aortic sinuses may be congenital syphilitic or mycotic Rupture of such an aneurysm into the pericardium or left pleural cavity is immediately fatal but perforation into the right atrium ventricle or pulmonary artery leads to a well defined clinical syndrome which may be compatible with many years of active life

Incidence

The condition is rare indeed the author has only encountered and investigated four living instances Congenital cases may occur in young adults syphilitic cases in later life and mycotic at any age About 80 per cent of reported cases have been in men aged 20 to 67 (Oram and East 1955)

Physiology

Rupture into the right atrium causes a large arteriovenous shunt into that chamber overloading of the right heart and the rapid development of congestive failure Cardiac catheterisation reveals a left to right shunt at atrial level Perforation into the right ventricle may similarly overload the right heart blood samples and intracardiac pressures are similar to those in ventricular septal defect (R A P 0 R V P 12 P A P 15 mm Hg S V C and R A samples 44 to 45 R V and P A samples 28 ml oxygen unsat per litre in a case seen by the author)



(a) Anterior view showing engorged pulmonary circulation enlargement of the left ventricle and resection of the 5th rib on the left side (the case having been operated on for patent ductus)



(b) Second oblique view showing enlargement of the left ventricle and dilatation of the pulmonary artery

Fig 20 02—Case of ruptured mycotic aneurysm of aortic sinus into the pulmonary artery

Perforation into the pulmonary artery sets up similar features to patent ductus arteriosus (fig 20 02) In one such case investigated by the author due to a perforated mycotic aneurysm from bacterial endocarditis (cured by penicillin) samples from the right atrium and ventricle showed 67 to 70 ml oxygen unsaturation per litre whereas pulmonary artery samples were only 33 to 36 ml unsaturated The mean right ventricular pressure was 31 mm of Hg above the sternal angle and the pulmonary artery pressure 63 mm Hg

Clinical features

Pain may occur from involvement of the orifice of one or other coronary arteries but is otherwise absent The onset is usually signalled by the rapid development of congestive heart failure but not necessarily The two cases mentioned above were by no means incapacitated and one is still alive 15 years after the onset

The chief signs are a loud machinery murmur accompanied by a thrill over the base of the heart but at a lower level than that associated with patent ductus arteriosus accompanied by signs of aortic incompetence and by features resembling those of ventricular septal defect or patent ductus according to the site of the perforation

Prognosis

Rapid deterioration to a fatal outcome is said to be the rule (Abbott 1919) but this may be because the diagnosis is usually only made at autopsy Three of the author s four cases are not only alive but relatively well the fourth died of heart failure

EFFECTS OF DIRECT INJURY

Direct injury to the heart may be caused by stab or gunshot wounds and very rarely by diagnostic procedures such as needling the pericardium The literature on the subject has been well surveyed by King (1941) and by Barber (1944)

GUNSHOT WOUNDS

A bullet or piece of shrapnel may perforate the heart through and through may lodge in the myocardium or pericardium with or without perforation of one or more chambers or may graze the surface of the heart without causing death In an analysis of 25 instances of war wounds involving the heart made in conjunction with Nicholson in 1945 the relative incidence of such lesions was as follows

Near misses	4
Grazes or tangential wounds	4
Through and through perforation	3
Foreign body in pericardium	7
Foreign body in myocardium	7

Of 1 640 consecutive penetrating chest wounds the heart was directly or indirectly injured in 1 7 per cent The immediate result is hæmopericardium and the rapid development of cardiac tamponade If a foreign body passes close to the heart or lodges within half an inch of its surface a transient pericardial serous effusion may develop If the patient does not die from cardiac tamponade or hæmorrhage into the pleural cavity complete recovery may follow whether or not a metallic foreign body remains in the heart

The chief complication during convalescence is recurrent acute pericarditis this is nearly always associated with the presence of a foreign body either in the pericardium or closely connected with it (Wood 1945) it rarely arises when a bullet is embedded deeply in the myocardium The attacks tend to be severe with pain fever tachycardia gross electrocardiographic changes and the rapid development of a sterile serous effusion which may cause cardiac tamponade They usually last about a week The first attack may occur at any time during convalescence up to about three months after the injury and may recur several times at intervals of about a month Of five such cases studied by the author in the second world war all finally recovered three without interference and two after removal of the foreign body by Nicholson (1945)

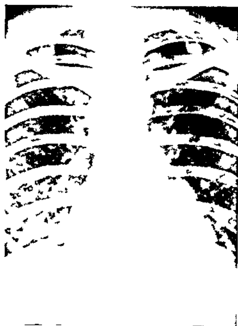

Fig 22 03—Machine gun bullet imbedded in the right atrium


Fig 22 04—Skiagram taken in 1937 showing machine gun bullet embedded in the heart since 1917

A second complication is coronary thrombosis during convalescence when a pericardial foreign body is in contact with a major coronary vessel but this was observed only once

Diagnosis The possibility of cardiac injury should be considered in all cases of gunshot wounds of the trunk or neck especially if the missile is judged to have been directed towards the heart or if its direction is not known for certain Early diagnosis depends upon recognising the signs of cardiac tamponade or hæmopericardium (page 661) An electrocardiogram may be most helpful by showing the presence or absence of the pericardial T pattern

Intracardiac or pericardial foreign body may be readily detected by means of fluoroscopy its movement with the heart beat aiding recognition but it may be easily overlooked in skiagrams

Treatment It is impossible to say how many lives might be saved by early surgical repair of cardiac wounds In the second world war the majority of cases that survived long enough to be evacuated to general hospitals recovered

Relief of cardiac tamponade by paracentesis may be life saving both in the early stages or during a later attack of acute pericarditis Metallic foreign bodies lodged in the pericardium are best removed in view of the danger of recurrent pericarditis Although none of the attacks witnessed proved

fatal the episodes were most alarming Intracardiac foreign bodies should probably be removed if superficial and left alone if deep

Prognosis Only one of the twenty five patients mentioned previously died but as already stated these were favourable cases in that they had survived until evacuated to a general hospital

Follow up studies are incomplete but the worst case with three attacks of recurrent pericarditis and a machine gun bullet embedded in the wall of the right atrium was alive and well two years after being wounded (fig 22 03)

In 1937 the author had the opportunity of investigating a healthy man with a machine gun bullet embedded in his heart since 1917 An unsuccessful attempt to remove the bullet was made at the time An electro cardiogram taken by Sir James Mackenzie showed the usual pericardial T pattern Twenty years later effort tolerance was excellent there were no abnormal physical signs and the electrocardiogram was normal X rays showed the bullet still embedded in the heart in close relationship to the apex of the interventricular septum (fig 22 04) This case was reported in detail by Grey Turner (1941) On the whole it seems likely that the ultimate fate of these patients is favourable

STAB WOUNDS OF THE HEART

Direct injury to the heart in civil life is usually due to single or multiple stab wounds the majority of which penetrate the right ventricle The clinical physiological radiological and electrocardiographic features of cases that have survived long enough to receive medical aid have been chiefly those of hæmopericardium (Wood 1937) Death from hæmorrhage into the pleural cavity or from cardiac tamponade may be prevented by timely surgical repair

Even when patients appear to be holding their own it is probably wise to evacuate the blood clot and to repair and sterilise the wound as soon as possible for hæmorrhage may continue or recur and serious cardiac tamponade develops in most cases Moreover if tamponade is unrelieved too long acute coronary insufficiency may seriously impair the function of the myocardium and when it is finally relieved death may result from acute heart failure The development of a bulge on the left border of the heart simulating the appearances of ventricular aneurysm should not deter the surgeon for this is likely to prove no more than a localised pericardial hæmatoma (fig 22 05)



Fig 22 05—Localised pericardial hæmatoma superficially resembling a cardiac aneurysm

EFFECTS OF INDIRECT INJURY

Indirect injury to the heart may be caused by crushes blows falls or blast The effects include sudden death from ventricular fibrillation or standstill rupture of the aorta rupture of one or more chambers of the heart rupture of the aortic or mitral valve, hæmopericardium myocardial bruising auricular fibrillation and heart block Coronary occlusion and subsequent angina pectoris or cardiac infarction may also occur but their relationship to trauma is less well understood

SUDDEN DEATH

A heavy blow to the region covering the heart may cause sudden death from ventricular fibrillation or cardiac rupture both naturally and experimentally in dogs (Bright and Beck 1935)

There have been numerous instances of sudden death resulting from relatively minor trauma of a kind quite incapable of damaging the heart The catastrophe is then ascribed to ventricular fibrillation or cardiac standstill induced by neurogenic shock Sudden immersion in icy water extreme fright or a blow over the heart insufficient to cause material damage may each act in this way This type of death is similar to that which may be caused by a small pulmonary embolism in experiments in dogs the size of the embolism being quite insufficient to embarrass the circulation and death being preventable by atropine The mechanism is probably a vagal reflex

Rupture of the aorta is more likely to occur from a fall, especially if there is congenital hypoplasia as in many cases of coarctation Hæmorrhage is usually into the pleural cavity or pericardium

RUPTURE OF THE HEART

Rupture of one or more chambers of the heart following trauma is not always immediate nor does it always cause sudden death A myocardial bruise may result in cardiac aneurysm or delayed rupture usually during the second week as described by Bright and Beck These authors collected over 150 cases of traumatic rupture of the heart from the literature and found the incidence of the various chambers involved to be as follows

Left ventricle	37
Right ventricle	31
Left auricle	30
Right auricle	36
More than one chamber	13
Interventricular septum	11
Interauricular septum	1

It will be appreciated that this distribution is very different from that seen with spontaneous rupture secondary to cardiac infarction when the left ventricle is nearly always responsible

The [illegible]tent interval was studied by Warburg (1938) It occurred in 15 out of 51 cases proved at necropsy A small tear may behave similarly to a direct penetrating wound that causes delayed death from hæmopericardium usually within a few days A bruise may rupture at any time within six weeks (Barber 1938) or occasionally after a longer interval Cardiac aneurysm resulting from a bruise may rupture years afterwards (Joachim and Mays 1927)

During the quiescent phase the patient may seem relatively well any discomfort being attributed to the bruise on the chest and he may continue his normal activities including sport (Priest 1939) In other cases symptoms may result from hæmopericardium or from any of the other effects to be described presently

Diagnosis

If the patient is seen alive after cardiac rupture the signs and symptoms are those of hæmorrhage into the pericardium or pleural cavity The combination of collapse rapid thready pulse and a high jugular venous pressure from cardiac tamponade is very suggestive if discovered within a month of injury There may be no evidence of external damage to the chest wall and the history of the accident may not be mentioned for it may not appear to be connected with the illness If the possibility of previous trauma is considered the diagnosis is usually obvious

Treatment

Immediate surgical repair is the only hope of saving life

HÆMOPERICARDIUM

Symptoms and signs of pericarditis with or without hæmopericardium are relatively common after indirect cardiac trauma particularly perhaps after blast injury They provide useful evidence of cardiac damage but do not necessarily indicate its nature Surgical interference is only warranted if there is tamponade which usually signifies cardiac rupture or serious coronary hæmorrhage Many cases have recovered spontaneously (Smith and McKeown 1939)

MYOCARDIAL BRUISING

Crushing of the chest direct blows over the heart and blast may all cause myocardial contusion the clinical picture resembling that of myocardial infarction including the characteristic electrocardiographic changes or heart failure without pain (Barber 1940 Barber and Osborn 1941)

Following a direct blow in the præcordial region, electrocardiographic changes may occur which are indistinguishable from those of posterior myocardial infarction (Anderson 1940) In these cases it may be assumed that the right coronary artery has been injured anteriorly

The chief danger of myocardial contusion is delayed rupture as previously described

Treatment consists of rest in bed for six weeks semi starvation a low sodium intake mersalyl if necessary sedatives, and avoidance of digitalis

RUPTURED AORTIC CUSP

Indirect trauma sometimes ruptures an aortic cusp There may or may not be underlying aortic valve disease congenital or acquired The lesion results in the abrupt development of aortic incompetence which throws a heavy burden upon an unprepared left ventricle so that failure of that chamber is likely to ensue

The diagnosis is suggested by the sudden onset of orthopnœa paroxysmal cardiac dyspnœa or pulmonary œdema following a serious fall or other violent accident and is confirmed by the discovery of a loud, harsh sometimes musical aortic diastolic murmur often accompanied by a thrill especially if the valve was known to have been normal previously

The prognosis may be good if the patient survives the immediate insult but death from heart failure within six weeks is a grave risk (Barber 1938 1944) Treatment consists of six weeks rest in bed in order to allow time for adequate compensation and may have to be directed towards combating left ventricular failure It must be understood that a degree of aortic incompetence which would be well tolerated and consistent with years of active life if it had developed slowly may cause death from acute heart failure when it occurs abruptly just as acute hypertension may cause left ventricular failure and pulmonary œdema whereas much higher pressures may be tolerated when developing slowly in benign hypertension

TRAUMATIC MITRAL INCOMPETENCE

A severe fall or sudden blow over the heart or other violent accident may occasionally rupture chordæ tendineæ or tear one of the mitral cusp particularly if already diseased The lesion is rare but there are many well authenticated instances (Barber and Osborn, 1937) A clinical diagnosis may be made from the history if it is known that no murmur was present before the accident if a loud harsh mitral systolic murmur is heard when the heart is first examined after the accident if there is no evidence of previous rheumatic valve disease and if confirmatory signs of organic mitral incompetence develop (page 506)

A number of cases have died from congestive heart failure within a few hours or weeks of the accident and others have developed mitral stenosis later (Barber, 1938) On the other hand the accidental discovery of symptomless mitral incompetence attributable to trauma need cause little alarm such cases behaving like rheumatic mitral incompetence with a healthy myocardium

HEART BLOCK

There have been a number of instances of asphyxia in which hæmorrhage has taken place around the bundle of His with resulting heart block Several

cases have been seen at necropsy by the author, and a good example was observed during the 1940–1 London air raids

A woman of about 35 known to have been in previous good health was rescued in a partly asphyxiated condition from beneath a lot of debris Examination shortly afterwards revealed not only complete heart block but also gross signs of hemi Parkinsonism presumably due to hæmorrhage into the bundle of His and into the substantia nigra She declared that she had received no severe blow on her chest nor significant crush but had been partly asphyxiated by dust for about one hour

Heart block may also result from a blow over the heart or from a fall on the chest (Coffen, 1930 Warburg 1938), and has been so produced experimentally in dogs (Kissane, 1937) Hæmorrhage into the conducting system is presumably responsible The lesion may be transient or permanent the prognosis depending on the presence or absence of Stokes Adams fits and upon the rate of the idioventricular pace maker, but on the whole it is *fairly good* provided there is no more serious injury and provided the heart muscle is sound

AURICULAR FIBRILLATION (OR FLUTTER)

Several cases of auricular fibrillation caused or precipitated by blows have been reported (Kahn and Kahn 1928) particularly in the elderly (Barber 1938) Bramwell (1934) records a case in which auricular fibrillation was probably initiated by a head injury, and Hay and Jones (1927) describe one due to electric shock

The mechanism whereby head injury may cause auricular fibrillation is particularly interesting though still obscure There is reason to believe that parasympathetic activity may be culpable Thus digitalis which stimulates the vagus, may cause auricular fibrillation and there is a form of sinus bradycardia due to vagal influence which is associated with paroxysms of flutter or fibrillation In experiments on certain animals fibrillation may be induced by vagal stimulation Not only head injury but also meningitis Meniere s syndrome and probably other intracranial disturbances may excite this rhythm change

CARDIAC INFARCTION AND ANGINA PECTORIS

As already described myocardial contusion may give rise to clinical and electrocardiographic features similar to those of myocardial infarction and may also result in cardiac rupture or aneurysm There appears to be a closer relationship however between trauma and ischæmic effects For example an anterior injury to the chest may cause a posterior left ventricular lesion clinically indistinguishable from a cardiac infarct and classical angina pectoris may develop for the first time immediately after trauma (Campbell 1939) Moreover the subsequent course of these cases may be that of ordinary ischæmic heart disease It is possible that blows crush injuries and blast may injure the anterior coronary vessels either by causing sub

intimal hæmorrhage in an atherosclerotic artery or more directly and thus cause acute coronary occlusion or secondary thrombosis After such an event subsequent angina pectoris would be readily understood Great care must be taken in diagnosing traumatic angina however, for many persistent chest pains following injury represent compensation neurosis

Treatment consists of three to six weeks rest in bed followed by one to three months convalescence to allow time for the development of adequate collateral vascularisation The prognosis depends upon the degree of underlying coronary disease as well as upon the amount of damage inflicted On the whole it is not dissimilar to that in ischæmic heart disease in general

MEDICO LEGAL ASPECTS

Employees are entitled to compensation if it can be shown that trauma has initiated or aggravated a cardiovascular disability Even a case of syphilitic aneurysm that ruptures during the course of work receives compensation Patients with established heart disease may deteriorate after an accident and this aggravation is equally compensated The benefit of doubt is always given to the patient and in a court of Law or a tribunal it is difficult to convince a judge or president that trauma has not adversely affected the cardiovascular system Yet a firm stand must be taken over the development of cardiac neurosis Left inframammary pain is especially liable to become persistent and intractable if linked to the idea of compensation and the physician must be prepared to make a categorical statement to the effect that this is not organic and is not due to the accident that it origin lies in the mind and in the emotions and its growth runs parallel with the conscious or subconscious desire for gain

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CHAPTER XXIII

CARDIOVASCULAR DISTURBANCES ASSOCIATED WITH PSYCHIATRIC STATES

THE cardiovascular system may be profoundly influenced by psychological or psychiatric states through the medium of the autonomic nervous system The stimulus is emotional and appears to act on the central vegetative nuclei in the region of the hypothalamus We are all familiar with the uncomfortable thudding of our hearts during moments of fear and most of us have witnessed a fainting attack provoked by the sight of something that is at once queer and frightening The physiological basis for such phenomena is relatively simple sympathetic or adrenergic activity may cause palpitations by accelerating the pulse elevating the blood pressure and strengthening the heart beat parasympathetic or cholinergic activity may induce syncope by retarding the pulse lowering the blood pressure and weakening the heart beat

Cardiovascular upsets of this kind sufficient to bring the patient to seek medical advice almost invariably indicate psychiatric disorder for the effects of emotion within the limits of common physiological experience are too transient and too familiar to disturb a normal individual Moreover in psychiatric states such symptoms may be persistent or may be provoked too readily The syndrome so produced has been called soldier s heart irritable heart disordered action of the heart (D A H) cardiac neurosis effort syndrome autonomic imbalance neurocirculatory asthenia etc Such terms should be discarded in favour of the correct psychiatric diagnosis but the words effort intolerance may be added with advantage preferably in brackets when clinically important Historically one may speak of Da Costa s syndrome to cover all previous nomenclature (Wood 1941)

The syndrome is characterised by a group of symptoms which unduly limit the subject s capacity for effort or which upset his peace of mind at rest by a number of signs which depend upon disturbance of the autonomic nervous system and by an underlying psychiatric disorder The cardinal symptoms are breathlessness (93 per cent) palpitations (89 per cent) fatigue (88 per cent) left inframammary pain (78 per cent) and dizziness (78 per cent) or syncope (35 per cent) The cardinal signs are those of functional disturbance of the respiratory vasomotor sudomotor and muscular systems The psychiatric disorder is commonly an anxiety state but may be almost anything with high emotional content including the psychoses

It should be understood that there is no essential difference between effort syndrome and cardiac neurosis they are merely clothed differ

ently the former in battle dress the latter in nylon In civil life the condition accounts for 10 to 15 per cent of all cases referred to cardio vascular clinics it is common in children and occurs more often in women than in men the ratio being 3 2 It has a preference for the emotional races especially the Jews and the Italians In the first world war there were some 60 000 ' effort syndrome casualties n the British forces in the second a more enlightened view was taken, the majority of these cases receiving appropriate psychiatric labels and management

CLINICAL FEATURES

The cardinal symptoms and signs have already been mentioned, they will now be discussed in more detail

Breathlessness These patients experience a true sensation of breathlessness in circumstances that would not affect a normal person It is not only a question of breathlessness on effort but patients will say they are unable to obtain a satisfying breath, or that they feel a sense of suffocation and this is confirmed objectively by frequent deep sighs Sometimes they complain of attacks of noctural dyspnœa which may be confused with bronchial asthma or with paroxysmal cardiac dyspnœa careful questioning however should reveal their psychosomatic nature especially by probing the precipitating anxiety dream and by unmasking the associated panic state Further evidence of functional respiratory disorder may be obtained by noting hurried irregular and shallow breathing A simple and illuminating test is forced hyperventilation The patient is asked to breathe deeply and rapidly for one minute A normal individual experiences dizziness and sometimes slight tingling of the fingers and toes When told to stop he passes into a state of apnœa lasting about 20 seconds The psychoneurotic especially the hysteric dramatises his subjective sensations and when told to desist usually continues forced breathing explaining later that he felt breathless Since dizziness is due to cerebral vasoconstriction induced by carbon dioxide washout it is clear that such psychoneurotics experience breathlessness when the carbon dioxide content of the arterial blood is so low as to cause apnœa in controls The respiratory stimulus must therefore come from higher centres The maximum breath holding time is another useful test Normal subjects have no difficulty in holding the breath for at least 30 seconds but patients with Da Costa s syndrome usually give up very quickly 30 per cent of them in less than 10 seconds moreover in contrast to controls they show little distress when they reach the breaking point

Palpitations Cardiac overaction resulting from emotional stimulation plays an important role in the induction of cardiac neurosis It is a common psychiatric event for some intangible fear to become linked to something more easily understood and remote from the real difficulty For example a psychoneurotic with a morbid fear of heights may develop palpitations

when ordered to climb a ladder If the idea that palpitations may denote some disorder of the heart occurs to him he at once embraces the possibility and proceeds to advance the theory in all seriousness for it disguises his true fear which might be thought shameful and protects him from the danger Although a successful defence mechanism in these two respects the manœuvre is baneful because it provokes a new fear that of heart disease and sudden death this new fear aggravates the palpitations and so closes a vicious circle

The palpitations of anxiety states are associated with sinus tachycardia elevation of the blood pressure increase in cardiac output and probably with strengthening of the heart beat These features are due essentially to emotional stimulation of a normal adrenergic system

Fatigue Patients often complain that they do not feel refreshed when they wake in the morning that their sleep has been of no benefit to them They also feel tired and listless during the day, and are unduly fatigued by effort The symptom is usually attributed to anxiety dreams and to emotional conflicts

Left inframammary pain Psychosomatic pain is usually situated in the left inframammary region but may be higher lower more central or more lateral it may radiate down the left arm It is commonly described as aching or as sharp and stabbing in quality but occasionally it is constricting or cramp like Although pain may occur during effort it is more frequent afterwards it is also common at night and may prevent the patient sleeping on the left side sometimes it is capricious and bears no relationship to any known factor Sharp twinges are momentary and acute stitch like pain may last several minutes but the classical ache usually continues for hours It thus usually differs from angina pectoris in its eccentric site its quality relationship to effort and duration i e in every important respect Occasionally however as may be inferred from the description given above psychosomatic pain may be situated near the left border of the sternum referred to the left arm constricting in quality and measured in minutes In such cases it may well be misinterpreted There is usually some odd remark however or something in the patient s manner which should warn the physician and encourage him to launch a critical cross examination The precise history of angina pectoris will not be shaken by this but that of an anxiety state alters and becomes more complicated and confused when elaborated

Left inframammary pain is important because it seems to convince the patient that his heart is diseased and it is not unnatural that he should think thus of a pain arising so close to it In the psychoneurotic this creates a morbid fear of death and catastrophe and so closes another vicious circle

The exact mechanism of the pain is obscure It is immediately abolished by the intramuscular injection of 2 ml of novocaine at the site of maximum intensity or tenderness Cutaneous or subcutaneous anæsthesia has no

effect This indicates that it is not referred but arises locally in muscle or fascia and suggests that it is related to 'fibrositis' and low back pain It may be initiated by fatigue or strain of respiratory muscles in cases with respiratory neurosis by strain of certain muscular attachments involved in such actions as cranking an engine or lifting a heavy weight, by incessant minimum trauma from the light hammer blows of an overacting heart or by faulty posture It is exaggerated and perpetuated by the belief that it arises in the heart

Dizziness Dizziness means momentary faintness, transient unsteadiness light headedness , or a far away feeling It does not refer to spinning as in vertigo It may occur on sudden movement of the head on standing up abruptly or during effort It is readily reproduced by hyperventilation when it is attributed to cerebral vasoconstriction Orthostatic dizziness is related to orthostatic hypotension, and is due to inadequate circulatory adjustments on assuming the erect posture It is probable that other forms of dizziness are also due to diminished cerebral blood flow induced by autonomic disturbance Transient loss of consciousness due to temporary failure of the cerebral circulation occurs at one time or another in 20 to 30 per cent of these cases

Sweating Sweating is a helpful diagnostic feature because in the majority of instances it is confined to the axillæ the palms of the hands and the soles of the feet These are emotional sweat areas Thermal sweating and that induced by cholinergic drugs, have a different distribution being much more widespread Sweating associated with effort may begin emotionally but is soon thermal Thyrotoxic sweating is also thermal The hands are the best single guide if sweating is confined to the palms the stimulus is emotional if the backs of the hands are also involved other causes should be considered Undue sweating is mentioned or admitted by 80 per cent of these cases and is seen objectively in about two thirds

Headache Headache is a common complaint (72 per cent) and is either vague or throbbing In assessing the reality of the physical basis of the throbbing type it is helpful to ask the patient to count the throb aloud or better to tap out the rhythm digitally while the observer checks this against the pulse rate in true vascular headache they must coincide in hysteria they do not Unilateral carotid compression is also useful for it abolishes vascular headache on the same side but it either aggravates or has no effect upon hysterical pain Throbbing vascular headache may be induced by the intravenous injection of 1 mg of histamine or by trinitrin or amyl nitrite in some cases It is closely associated with exaggerated pulsation of the cerebral arteries (Pickering 1939) It is seen clinically not only in the anxiety states but also in fevers and in acute alcoholism It occurs spontaneously in migraine Improvement depends upon better autonomic regulation, which in turn depends upon successful treatment of the underlying anxiety state



Fig 23 01—Clas ical facies build and posture of a case of Da Costa s syndrome Painted by Ian Tillard (l fe size portrait in the museum of the Post Graduate Medical School of London)

PHYSICAL SIGNS

Signs of autonomic disturbance serve to check the validity of psycho somatic symptoms Most have already been mentioned but they will be recapitulated and grouped here for convenience

General
- Tense dejected or diffident manner
- Dull weak or listless facies
- Soft quiet timid voice

Cardiovascular
- Tachycardia (30 per cent)
- Overaction of the heart (44 per cent)
- Blood pressure in the region of 150/90 mm Hg (27 per cent above)
- Deceleration time over 2 minutes in effort tolerance test (33 per cent)
- Acrocyanosis (44 per cent)
- Flushes (36 per cent)

Respiratory
- Frequent deep sighs (32 per cent)
- Rapid irregular or shallow breathing occasionally hyperventilation (21 per cent)
- Inability to hold the breath for 30 seconds (76 per cent)
- Dyspnœa instead of apnœa after forced breathing

Sudomotor
- Visible sweat on the palms of the hands (67 p r cent)
- Sweat trickling from the axillæ (35 per cent)

Skeletal and Muscular
- Tremor of fingers usually coarse irregular and inconstant (6 per cent)
- Shakiness of voice and limbs
- Asthenic posture or poor physical development (41 per cent)
- Tenderness in area of left inframammary pain

A life sized portrait of one of these patients (fig 23 01) hangs in the library of the Postgraduate Medical School of London and surpasses any description The effort tolerance test consists of stepping on and off a chair ten times and counting the pulse rate before immediately after and subsequently at minute intervals until the resting speed is regained The deceleration time is abnormal (over 2 minutes) in 33 per cent of these patients

Physical signs of autonomic disturbance are helpful in distinguishing the malingerer and in assessing the severity of the case About 90 per cent of normal young adults do not show more than one of these signs and 50 per cent show none

PSYCHIATRIC ASPECTS

Although the syndrome described may occur in any psychiatric state with high emotional tone it is usually associated with an anxiety state In many there are hysterical features and a large number show reactive depression

The family history is tainted with psychoneurosis in 50 to 60 per cent compared with 5 to 10 per cent in controls with or without organic heart disease About 66 per cent describe neurotic traits in childhood morbid fears especially of the dark of heights of water or of animals are frequent bed wetting stammering tics nightmares sleep walking and undue delicacy of health are common They are timid children far too dependent upon maternal protection At school kindly doctors and soft mothers protect them from the hazards of football swimming and the gymnasium

It is probable that predisposition to psychoneurosis is mainly hereditary but early environmental factors such as domestic strife insecurity suppression and maternal coddling play their part

There are many factors which may operate to bring about the adult syndrome and in any particular case one should never be satisfied with the discovery of only one or two It is fruitful to search for evidence of predisposition for a state of mind recently prepared for the development of psychoneurosis by external or by endogenous factors for precipitating agents for the growth of vicious circles and for motives for gain that aggravate and perpetuate the syndrome Proper assessment management and prognosis are impossible if any vital link is overlooked

Hereditary and environmental predisposition have already been discussed *The mind is especially prepared for the development of psychoneurosis* when in a state of confusion and unreality Head injuries may bring this about certain acute fevers are often responsible especially rheumatic fever influenza meningitis and diphtheria long hours of work in unpleasant and unhappy surroundings may be to blame

Precipitating factors are often multiple It is as if one or two could be coped with but when several occur one on top of the other mental equilibrium disintegrates They are usually closely linked with fear in some form or another The most obvious example is active service hence the high incidence of the disorder in war Fear of football and fear of swimming are common in childhood and may precipitate anxiety at school The fear of being unsuccessful of not being able to shoulder responsibility is a common cause of breakdown in civil life Insecurity or fear of the future is also common The adoption of a line of action contrary to established social custom may cause an anxiety state due to fear of discovery and public criticism Difficult personal relationships especially between husband and wife are often responsible Sex difficulties are important, but should not be over emphasised Financial worry unemployment fear of disease play their part To a timid sensitive character the

being found out of being thought a coward, of being proved inadequate of seeming a fool—and so of losing cast, is a very real and powerful emotional stimulus

The *development of vicious circular patterns is interesting* In this particular syndrome most vicious circles have a common basis and revolve round the fear of heart disease and sudden death The combination of breathlessness dizziness or syncope fatigue and especially palpitations and left inframammary pain provides convincing evidence of heart disease to the lay mind All these symptoms which are psychosomatic in mechanism may be produced by simple anxiety and may disappear rapidly as soon as the anxiety is resolved But if the patient takes the fatal step and believes that they are due to heart disease a vicious circle is at once established for a new and greater fear develops that of sudden death at any moment This constant anxiety operating consciously or subconsciously every second of the day and night increases the severity of the psychosomatic symptoms Under these circumstances the syndrome is maintained long after resolution of the original anxiety Superimposed upon this pattern or independent of it there develop various and often complicated conditioned reflexes until finally distressing autonomic reactions are so ingrained and so divorced from conscious thought as to be practically ineradicable Correct medical interpretation of early psychosomatic symptoms is of the utmost importance in the prevention of these pernicious grooves The doctor who misinterprets a boy s fear of water and accepts the pallor and palpitations as signs of heart disease who mistakes left inframammary pain for angina pectoris who finding an innocent systolic murmur diagnoses valvular heart disease who regards syncope or dizziness as a sign of cardiac weakness is guilty not only of stupidity and ignorance but is also responsible for turning his patient into a chronic and incurable psychoneurotic Even so it may be comforting to know that medical blunders of this kind will influence only 10 per cent of apparently normal individuals the great majority adversely affected showing evidence of predisposition

Finally *there* is the motive for gain This is seen in compensation neurosis and in war it is obvious at every medical board The inadequate personality of so many of these patients capitalises the symptoms What timid man indifferent to higher ideals will face the dangers of battle when the very symptoms of his fear offer him protection?

DIFFERENTIAL DIAGNOSIS

The characteristic symptoms and signs associated with psychiatric disorder usually make the diagnosis easy The physical features have been stressed because the psychiatric state may not be obvious until the mind has been deeply probed This is well shown by comparing the conclusions drawn at the special investigation centres for effort syndrome during the

first two world wars at Hampstead in world war I where little attention was paid to psychiatry not more than 10 per cent were considered psychoneurotic at Mill Hill in world war II a psychiatric basis was proved in 94 per cent The diagnosis should be positive not dependent upon a process of exclusion it may stand even when organic disease is also found especially mild rheumatic heart disease benign hypertension and chronic bronchitis

Thyrotoxicosis may present difficulty to the inexperienced The common mistake is to diagnose an anxiety state as thyrotoxicosis rarely the reverse The difference is fully considered on page 874 and 878 Particular attention should be paid to the attitude and behaviour of the patient to the expression of the eyes to the colour and temperature of the hands to the distribution of sweating to the diastolic blood pressure and to the appetite

In children active rheumatic carditis may cause confusion vague muscle pains being mistaken for joint pains and tics for chorea

Attacks of violent palpitations in anxiety states are sometimes confused with paroxysmal tachycardia Accurate history taking and observation of an induced attack should prevent error The special points of difference are given on page 237

The distinction between left inframammary pain and angina pectoris has already been considered but real difficulty may arise In both the diagnosis depends largely upon the history and cannot be proved or disproved by the demonstration of psychoneurosis on the one hand or of organic heart disease on the other The matter is further complicated by the adverse effect of anxiety upon ischæmic heart disease for it may be so important a factor that its satisfactory resolution may temporarily relieve angina pectoris Occasionally the diagnosis remains doubtful until determined by the future course

The physician should be on his guard against pulmonary tuberculosis chronic undulant fever juvenile spondylitis spontaneous hypoglycæmia and certain endocrine disorders—especially the menopause Anæmia should be more obvious When the symptoms first arise during convalescence simple reassurance should be given and the final diagnosis deferred until it is clear that rapid recovery has or has not taken place

TREATMENT

Treatment is never easy and is the more difficult the longer it is delayed Failure is certain if any essential factor in the development of the syndrome is overlooked so that a great deal of time must be spent on these patients Simple reassurance and some superficial explanation are quite inadequate

First the patient must feel that at last he has met a doctor who thoroughly understands his case secondly a complete physical examination supp by fluoroscopy and an electrocardiogram is necessary so that

respect unconditional reassurance Adequate explanation must follow, and will vary according to the chief symptoms The object is to convince the patient that the symptoms are emotionally produced One may point out how sudden fear causes palpitations sweating alteration of breathing and sometimes a fainting attack He will agree with this but may object that he feels no such fear One should then explain that great fear acting for a few seconds may be more than equalled by a tiny remote fear acting over weeks months or years a state called anxiety This step is difficult but the point must be carried Correct interpretation of anxiety dreams is of value in demonstrating the power of subconscious emotion Enlightenment and conviction may come suddenly if psychosomatic disturbance on some particular occasion or under certain specific circumstances can be explained in the light of emotional experience

For example a patient at Mill Hill gave a history of a morbid fear of fireworks in his boyhood conditioned by London air raids in his infancy Otherwise he was fit and strong He was called up in September 1939 was sent to France and remained well until told one day to unload an ammunition lorry On handling the shells he became curiously panic stricken developed gross psychosomatic symptoms and mis interpreted them thinking they meant heart disease A vicious circle was initiated he reported sick and finally arrived at a base hospital with an established effort syndrome When the link between his fear of handling fireworks and his handling shells for the first time was pointed out he was suddenly convinced of the truth of the explanation given for his symptoms and made a rapid and complete recovery But his fear of fireworks shells and all other explosives was unabated Treatment had only been directed towards the removal of effort intolerance by abolishing the misinterpretation and vicious circle that initiated and maintained it

As a rule however it is not enough to reassure and give an adequate explanation for by the time the patient consults a physician the syndrome is usually highly complex and conditioned reflexes are well ingrained To cut across such reflexes and vicious circles, one may encourage the patient to come to better terms with his symptoms He fears them because he thinks they are injurious and may result in sudden death He must be told they are harmless that they can never be more than a nuisance that he is already familiar with the worst they can do Once he appreciates the fact that if he no longer fears his symptoms he will cease to aggravate them the point is scored

If there is an hysterical motive for gain it must be mentioned and then ruthlessly underlined It is remarkable what little insight these patients have, and disconcerting how little shame

The methods so far outlined do not touch the underlying psychoneurosis and the real treatment has yet to begin The patient may be referred to a psychiatrist or if the causative factors seem clear the physician may prefer to deal with them himself There are always three things to consider the difficulties in which the patient is floundering his reaction, which is based

on his character and intelligence and his attitude towards his reaction The difficulties should be taken first sorted out and resolved as far as possible The help of social welfare workers may be enlisted in this respect The patient s reaction should be analysed and some psychiatric skill and knowledge are required to do this It is often possible to show that his reaction is based on false values ideas or beliefs Or one may simply explain just why he so reacts in order to give him insight It is impossible to outline precisely just what is required for every case is different and needs individual treatment If the problem has no satisfactory solution and if the patient s reaction cannot be altered favourably then at least he may learn to get on better terms with both Difficulties must be faced and not hidden away in the dark recesses of the mind highly personal matters should be fully discussed in a matter of fact way until they cease to seem so dreadful if a man is standing on a false pedestal he must learn humility and honesty and tread upon the good earth

Finally the background must be assessed With strong hereditary taints and bad early environment the outlook is poor and the aim should be to fit the patient into circumstances which will cause the least embarrassment This is a confession of failure At the other extreme if the stock is good and if there is no evidence of predisposition and if this is confirmed by the severity of the stress of anxiety causing the breakdown every effort should be made to cure the patient In other words one should deal with the environment when the prognosis is bad and with the patient when it is good

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may be given in the use of an atomiser of the de Vilbiss pattern charged with protargol 10 per cent Internally, expectorants are indicated, tinctura ipecacuanhæ, min 10, or vinum antimoniale min 5 potassium iodide gr 2 or 3 ammonium carbonate gr 4, every 4 or 6 hours If cough is severe it should be restrained by means of a tincture containing codeine phosphate gr ⅛ or liquor morphinæ min 2 to 4 to each drachm

ŒDEMATOUS LARYNGITIS

Synonym —Œdema of the Larynx

Ætiology —Œdema of the larynx is not a disease but a pathological condition due to a variety of causes Non inflammatory œdema may be mentioned here for the sake of completeness, it occurs, though rarely, as part of the general anasarca of renal and cardiac disease Angio neurotic œdema sometimes occurs in the larynx in which event it produces rapid and sometimes fatal dyspnœa (see p 1255) The swelling which occasionally results from administration of potassium iodide in susceptible subjects may be placed in the same category

Inflammatory œdema seldom results in adults from a simple catarrh but it may do so in children, it more often occurs as part of an acute septic infection of the pharynx, trachea and bronchi ' acute fulminating laryngo tracheo bronchitis ' (*q v*) Œdema may follow various forms of trauma the drinking of corrosive poisons inhalation of irritating vapours such as the poison gases of warfare the lodgment of foreign bodies or rough or unduly prolonged bronchoscopy Scalding from attempts to drink from a kettle spout is a common cause among children In other cases it is a sequela of typhoid fever, pneumonia, scarlet fever or small pox and is a local complication of syphilitic tuberculous cancerous or traumatic ulceration

Symptoms —If part of a septic pharyngo laryngitis the general symptoms are severe The chief local symptom is dyspnœa with inspiratory stridor and the associated symptoms of asphyxiation there is hoarseness or aphonia local discomfort and tenderness and sometimes dysphagia The aryteno epiglottidean folds are enormously swollen appearing as pale or purple translucent flask shaped masses, if the epiglottis be œdematous it forms a sausage shaped swelling of the same appearance The mucosa of the vocal cords is too adherent to permit much swelling and œdema of the glottis is therefore a misnomer The subglottic region is lax and may become swollen indeed the œdema may be confined to this region and then appears as a red swelling below each vocal cord In children œdema may be inferred from the steadily increasing dyspnœa without the rapid increase and decrease typical of spasmodic laryngitis

Treatment —Patients should be nursed in a semi sitting position In slight cases the swelling may be reduced by sucking ice and by the application of an ice bag to the neck the latter is inadmissible in young children A spray of adrenaline 1 in 1000 may be used Hypodermic injections of pilocarpine, gr ⅛ are recommended, and for the œdema produced by iodides large doses of bicarbonate of soda When œdema is the result of an acute streptococcal infection full doses of sulphonamides and penicillin should be given without delay Scarification of the œdematous tissues with a curved bistoury which was accepted practice in the past is now not recommended because of the disturbance it causes to patients the danger of blood entering the trachea and the chances of giving rise to secondary infection Tracheotomy should be performed before respiratory embarrassment is too great intubation is not recommended Angio neurotic œdema should be treated by a spray of adrenaline but as this condition is often allergic in origin it is logical to prescribe full doses of one of the anti histamine drugs such as promethazine or phenindamine Intravenous calcium gluconate is excellent treatment Very rarely tracheotomy may be necessary

MEMBRANOUS LARYNGITIS

The formation of false membrane in the larynx is nearly always part of an attack of diphtheria which is discussed elsewhere but the term membranous laryngitis implies formation of membrane of non diphtheritic origin Apart from traumatic cases due to irritating chemicals and scalds inflammation of the larynx accompanied by membrane may be caused by streptococcal infection The affection occurs especially in children between the ages of 2 and 8 years (see Acute Laryngo-Tracheo Bronchitis p 946) The diagnosis from diphtheria is only possible by bacteriological examination and pending the report the case should be treated with antitoxin It may be noted that the pharynx is nearly always involved in diphtheria whereas in membranous laryngitis the disease is often primary in the larynx The prognosis is grave and worse than that of diphtheria since the introduction of antitoxin

ACUTE LARYNGEAL CONDITIONS AFFECTING CHILDREN

In the past it has been customary to describe a group of acute laryngeal conditions occurring in early childhood all of which are associated with dyspnœa A great deal of unnecessary confusion has arisen because there has been (and still is) some uncertainty as to the mechanism of such conditions An unfortunate nomenclature has been evolved which is muddling and unhelpful

An attempt will be made to clarify the situation by confining description to acute laryngitis in children acute laryngo tracheo bronchitis congenital laryngeal stridor and laryngismus stridulus

For years the expression croup has been used so universally that many have wrongly supposed that the term denoted a definite disease The word dates from a period when diagnosis of diseases of the throat was far from exact and the meaning was obstructive dyspnœa The adjective croupy may still be used to describe noisy inspiratory stridor, itself a symptom of diverse laryngeal affections

ACUTE LARYNGITIS IN CHILDREN

In young children the larynx is small whilst the cartilages are soft and yielding The mucosa is rather loosely connected to subjacent tissues so that effusion can take place more readily It seems that the controlling nervous mechanism is somewhat unstable and that glottic spasm is more easily evoked For these reasons laryngitis in children is always a serious condition and alarming symptoms especially dyspnœa and cyanosis may develop with extreme rapidity A child save for a slight cough may seem well during the day and then at night may suddenly develop laryngeal spasm and become seriously ill Acute laryngitis with spasm is a better name than the old established laryngitis stridulosa a term which though accurate enough has served to confuse generations of medical students

Treatment—The time honoured treatment has been an emetic and a purge Emetics are certainly helpful in some cases and tincture ipecacuahnæ min 60 may assist in the removal of obstructing secretions An aperient may be given remembering that there is no specific virtue in calomel It is well to put up a steam kettle and there are occasions when oxygen will be required Antibiotics will not directly relieve laryngeal spasm but may be indicated to control the primary infection Very rarely indeed is tracheotomy required When the acute attack has passed the child should be examined with a view to eliminating unhealthy adenoids or tonsils

ACUTE LARYNGO TRACHEO-BRONCHITIS

Ætiology —This severe disease *usually occurs* in children under 3 years of age and is rarely seen after the age of 6 Weakly children are most often affected and the mortality even now is about 15 per cent The responsible organisms may be streptococci, staphylococci pneumococci or influenza bacilli There is redness and swelling of the arytenoid region and gross subglottic swelling which spreads down into trachea and bronchi An exudate is poured out into the tracheo bronchial tree and quickly becomes thick and tenacious, its expectoration is often beyond the strength of the patient Pneumonia and atelectasis from plug formation form a prominent part of the clinical picture

Symptoms —*In most* cases the disease *develops* comparatively *slowly*, *only* occasionally is an infant rapidly prostrated The following graphic description is quoted from F C Emery As the disease progresses these patients become de hydrated prostrated and finally present a picture of complete collapse The cyanosis disappears leaving an ashen pale skin and anoxic coma, with all the remaining energy being spent on breathing Retraction may be so great that the sternum and thoracic spine seem to meet with each gasping inspiration '

Treatment —Humidification of inspired air is important and a steam kettle can be used with advantage Almost all cases must be at some time nursed in an *oxygen tent a mixture of helium and oxygen has been recommended by Jackson* Sleep is a grave problem as drugs given to ensure sufficient rest *damp down* the cough reflex On the other hand continual coughing may so sap the patient s physical strength that some opiate must be given In theory causative organisms *should be* isolated and tested for sensitivity to the various antibiotics and sulphonamides *but* time should not be wasted whilst waiting for the bacteriologist s report Penicillin is generally u eful but evidence is mounting which suggests that *chloramphenicol is* substantially more effective Every effort must be made to *keep up the fluid* intake

Bronchoscopy often becomes an *urgent* necessity for this may be the only practical method of ridding a patient of tenacious secretions and pseudo membranous *sloughs* Sometimes even this procedure is inadequate and an emergency tracheotomy is indicated It must be remembered that obstruction to respiratory exchange may be as great below the tracheotomy as above it but an opening in the trachea *facilitates* lavage and suction

CONGENITAL LARYNGEAL STRIDOR

In this condition there is an exaggeration of the *infantile* shape of the upper *aperture* of the larynx *the epiglottis is sharply* folded laterally the ary epiglottic folds are almost in contact and the opening is thus reduced *to a narrow* vertical slit As these parts are very flaccid in infancy they become sucked together during in spiration and by their vibration produce the characteristic stridor This stridor is noticed very soon after birth it is inspiratory of a *peculiar purring* or even musical character, and is most marked during active breathing *and crying The voice is* unaffected and there is remarkably little sign of dyspnœa or distress These char *acteristics distinguish the condition from other forms of obstruction* found in infants such as laryngeal web or papillomata or thymic asthma Symptoms tend to disappear during the second year of life but the prognosis must be guarded in early infancy for an attack of bronchitis is more than o *dinarily* dangerous and kills a proportion of these patients

LARYNGISMUS STRIDULUS

Ætiology —This is a condition clinically similar to glottic spasm occurring in children It is far commoner than the spasm of adults and it has been suggested that the asphyxial attacks of laryngismus are caused by collapse of the soft and yielding cartilaginous framework of the larynx and not solely by spasm of the muscles It is commonest between the ages of 6 months and 2 years but may persist later it occurs in ill nourished unhealthy children often in association with rickets and practically always in association with adenoids

Symptoms —The onset is sudden and attacks usually occur at night The child wakes gasping for breath and a series of short noisy inspirations is followed by complete cessation of breathing a long crowing inspiration terminates the attack There are retraction of the lower ribs and epigastrium cyanosis and great terror and distress and in severe cases carpo pedal contractions convulsions and evacuation of urine and fæces When the attack is over the child is perfectly normal and there is no hoarseness Slighter and less typical attacks often occur

Diagnosis —This is easy if the symptoms are carefully noted the sudden attack of dyspnœa with complete absence of symptoms in the intervals is quite distinctive

Prognosis —The prognosis is somewhat grave in severe cases an infant rarely dies in an attack but is often worn out and eventually succumbs to collapse of the lungs

Treatment —During the attacks the face and chest may be freely sponged with cold water and the inhalation of amyl nitrite from a capsule broken in a handkerchief may be tried The child should be supported sitting up and the quickest relief can usually be obtained by drawing the tongue forward with a finger passed into the mouth to its base a manœuvre easily performed by the mother or nurse The attacks are so short and sharp that there is no time for the hot bath or administration of bromides frequently recommended

Prevention involves the control of rickets with vitamin D fresh air wholesome food and correction of digestive disturbances Attention should be given to eliminating infection in the nose and drops of protargol 2½ per cent , may be instilled when the child is in the head down position It is particularly important to remove adenoids even if they are only moderately enlarged

CHRONIC LARYNGITIS

Ætiology —The causation is similar to that of acute catarrhal laryngitis indeed chronic laryngitis is often the result of recurrent acute attacks The principal factors which predispose to chronicity are nasal obstructions and discharges dental infections and chronic tonsillar sepsis dusty occupations and lack of fresh air over use of the voice and faulty voice production and the abuse of alcohol or tobacco consumptives are particularly liable to non specific catarrhal laryngitis Almost any cause of general ill health may be included among the predisposing causes

Symptoms —The only constant symptom is impairment of the voice which is hoarse easily tired or rarely almost completely lost It is sometimes weakest when tired in the evening but is often at its worst on rising in the morning or after a rest There is frequently a sensation of aching dryness tickling or of a lump in the throat and there is usually some cough but little expectoration unless the trachea and bronchi are involved

The objective appearances vary with the severity of the affection The larynx generally is of a deeper red than usual and the vocal cords have lost their normal pearly lustre and are pink they are usually somewhat thickened at the edges and enlarged vessels may be visible on their surface the vocal processes are often prominent and may be reddened or show up white against the hyperæmic cord Strings

of sticky secretion may stretch between the cords or a little globule of mucus may form on the centre of the cord during phonation, adduction is frequently imperfect When the epiglottis is reddened, its yellow edge stands out clearly and enlarged vessels are visible the ventricular bands are often swollen so as to hide the outer part of the cords The mucous membrane in the inter arytenoid space is seen to be thrown into folds on adduction of the cords and may form a mass large enough to prevent their complete approximation The general picture is one of symmetry a useful point in diagnosis when tuberculous laryngitis is in question

A patient suffering from atrophic rhinitis may develop an unusual form of chronic laryngitis known as *laryngitis sicca*, in which small brown scabs adhere to the cords and posterior commissure, but occasionally the disease itself spreads to the larynx which is covered by large greenish or brownish black fetid crusts, more rarely still the crusts extend into the trachea and cause severe dyspnœa

Pachydermia laryngis is an uncommon variety of chronic laryngitis occurring principally in middle aged men It is frequently ascribed to alcoholism, though perhaps on insufficient grounds and the diagnosis between pachydermia and tuberculosis or syphilis is often a matter of difficulty The characteristic epithelial thickenings are probably of the nature of corns resulting from frequent cough and continued irritation There is hoarseness of a rough raucous character, but no particular discomfort The epithelial thickening is pink or whitish and occupies the posterior region of the glottis from the vocal processes backwards to the posterior commissure A circumscribed swelling appears on each vocal process, with a small cup or depression at the apex the approximation of the cords is better than would be expected because the prominence on one vocal process fits into the depression at the other The epithelium of the inter arytenoid space is thrown into ridges which fill up the angles between the arytenoid and the posterior commissure but leave a depression in the middle line These firm opaque symmetrical swellings without ulceration are distinguishable from the soft irregular granulations of a tuberculous lesion

Treatment —The detection and correction of the ætiological factors are the most important part of treatment Any constitutional disturbance, such as anæmia rheumatism gout or dyspepsia should receive attention Over indulgence in tobacco or alcohol lack of ventilation and exposure to dust must be considered, and with teachers the blackboard chalk is a common source of irritation

Incorrect voice production is a factor of great importance and a good speech therapist can often provide substantial help

Almost always some infection is discovered in nose sinuses tonsils or teeth Elimination of such infection is the most important step in treatment

Locally treatment must begin with rest of the voice which should be absolute in the case of professional voice users Where there is much secretion a saline lotion may be used in a spray—sodium bicarbonate borax sodium chloride, gr 10 of each glycerin 60 min water to 1 oz Oily solutions are usually preferred such as menthol gr 5 camphor gr 2 chlorbutol gr 5 or oil of eucalyptus in similar proportions to 1 oz of liquid paraffin The direct application of pigments is not often called for and is to be recommended only when pachydermatous changes are present Dundas Grant advised an alcoholic solution of salicylic acid beginning with 1 per cent and increasing to 6 or 8 per cent

Internally small doses of potassium iodide, gr 2 or 3 three times a day over long periods is of value

TUBERCULOUS LARYNGITIS

Ætiology —In all cases the disease is secondary to pulmonary tuberculosis, of which it is an important complication It is probably caused by infection from the

sputum, is commoner in men than in women and is most frequent between the ages of 20 and 40 St Clair Thomson found that the difference in sex incidence is occupational and that women working in office and factory are as susceptible as men

Symptoms —The disease attacks in order of frequency the vocal cords arytenoid region inter arytenoid space ventricular bands and epiglottis in general the glottis is invaded before its upper aperture The typical infiltration is finely nodular pallid and soft in appearance ulcers are shallow with a smooth speckly base and pale ill defined margin On the vocal cord the disease chiefly attacks the posterior half and especially the vocal process where ulceration readily reaches the underlying cartilage and may produce a deep triangular excavation Thickening in the inter arytenoid region is common infiltration of the ary epiglottic folds results in typical pale semi translucent flask shaped swellings while the epiglottis appears as a firmer red sausage shaped mass

The voice is weak and has not the raucous quality associated with syphilis Sometimes voice production is actually painful Cough and expectoration are mostly due to the pulmonary disease and not in any considerable degree to the larynx Pain on swallowing is common and often very intense there may also be actual obstruction to deglutition and in a late stage entry of food into the larynx Dyspnœa is rare

Diagnosis —Although signs of pulmonary tuberculosis are helpful in diagnosis it is obvious that any kind of laryngeal disease may occur in a consumptive patient

From simple laryngitis —In the earliest stage of invasion tuberculous laryngitis may exactly resemble catarrhal laryngitis but redness of one cord only is certainly not due to catarrh and the latter quickly improves under treatment Inter arytenoid infiltration resembles pachydermia but the latter is opaquely white firm and symmetrical

From lupus typical tuberculosis differs completely The former is painless affects first the epiglottis and upper aperture is never accompanied by œdema and tends to cicatrisation But there is a chronic lupoid form of tuberculous laryngitis which attacks the epiglottis and is very similar to lupus

From syphilis —The tuberculous ulcer has an ill defined margin without surrounding hyperæmia the base has a yellow speckled appearance and on healing there is little scarring or contraction The superficial syphilitic ulcer has a well defined hyperæmic margin with a smooth flat base the deep ulcer is crateriform with thickened punched out edge and on healing leaves a dense scar and marked deformity In general syphilitic lesions attack the anterior half of the larynx tuberculous the posterior the former look firm and dense the latter soft translucent and ill defined

From neoplasms —Only the rare tuberculomata resemble innocent tumours Occasionally tuberculosis attacks one vocal cord in an elderly patient and may then easily be mistaken for epithelioma especially when as often happens in such cases, the pulmonary signs are inconclusive and tubercle bacilli absent from the sputum

Prognosis —This has greatly improved in recent years due to advances in the chemotherapy of tuberculosis

Treatment —Tuberculous laryngitis is but a complication of pulmonary tuberculosis and by far the most important part of the treatment is that of the general infection Complete vocal rest has in the past been the mainstay of treatment this is a severe and depressing measure and it is now not always necessary to enforce complete silence Streptomycin combined with isoniazid or sodium aminosalicylate (P A S) not only promotes healing of laryngeal lesions but within a very short time abolishes pain and dysphagia It should now never be necessary to use a galvano cautery or to insufflate analgesic powders let alone to inject alcohol around the internal laryngeal nerve In these days one no longer sees the desperate case of tuberculous

laryngitis in which the airway becomes obstructed and tracheotomy is called for There have, however, been rare cases of cicatricial stenosis following 'successful" chemotherapy

PARALYSIS

Paralysis of a vocal cord occurs in association with various diseases of the thorax and of the nervous system The early form unilateral abductor paralysis, causes no symptoms and can only be recognised by laryngoscopic examination

The original function of the laryngeal muscles is that of a sphincter to prevent the entrance of fluid into the lungs, and this sphincter or adductor, is the only muscle present in the larynx of primitive air breathing animals the abductors are a later addition In progressive lesions involving the nerve pathways the abductor muscles are first affected whilst the adductors continue to function for a variable time The function of phonation, much more recently acquired is associated with adduction and is under direct control of the will Functional disturbances therefore always cause adductor paralysis, while organic lesions first affect the movement of abduction

ORGANIC PARALYSIS

The crico thyroid muscle is supplied by the superior laryngeal nerve, and when this is injured the affected cord remains slack on phonation but owing to the short course of the nerve isolated paralysis of this muscle is extremely rare it results from surgical or suicidal wounds, and may occur after diphtheria In lesions of the vagus above the origin of this branch the signs of this paralysis are obscured by that of the other muscles of the cord The recurrent laryngeal nerves supply all the other muscles In any progressive lesion of the nerve pathway the muscles become paralysed in a definite order the abductors are first affected then the internal tensors or thyro arytenoidei and finally the adductors This is known as Semon s Law

There is but one muscle on each side which acts as an abductor of the vocal cord namely the crico arytenoideus posticus (often for convenience alluded to as the posticus muscle) This muscle not only moves the vocal cord away from the mid line during respiration, but its most posterior fibres brace back the arytenoid cartilage and stretch the aryepiglottic fold The cartilage of Wrisberg is incorporated in the fold and helps keep it taut in an upright position Thus it is that in ' posticus paralysis the aryepiglottic fold droops inwards and the cartilage of Wrisberg tilts forwards and inwards with it Yet another thing happens the arytenoid cartilage is free to slide and tilt forwards so that the cord appears shortened and tends to lie at a slightly lower level This forward tilting and apparent prominence of Wrisberg s cartilage is of help in diagnosis

ABDUCTOR PARALYSIS

The affected cord lies immobile in the midline, being held there by the unopposed action of adductor muscles (crico arytenoideus lateralis and inter arytenoideus) On phonation the unaffected cord swings over to meet its immobile fellow so that the voice is unaltered It is not quite true to say that during phonation the larynx appears normal for on the sound side Wrisberg s cartilage seems to move forward in front of its fellow The glottic aperture is reduced but dyspnœa is only noticed on exertion

Bilateral abductor paralysis is a serious condition particularly if the onset is sudden as both cords lie together in the middle line leaving a mere chink Inspiratory

embarrassment is extreme but the conical shape of the subglottic region allows expired air to blow the glottis open The voice is quite good, though the patient must constantly pause in a vain attempt to fill the lungs Were it not for forward displacement of the arytenoid cartilages referred to above thus allowing a chink patients would asphyxiate

COMPLETE PARALYSIS

When only the recurrent laryngeal nerve is involved the affected cord assumes a ' paramedian position for the crico thyroid muscle an external tensor and weak adductor is still acting The cadaveric or intermediate position can only be assumed when this muscle also is paralysed as in a lesion of the main vagus trunk above the superior laryngeal nerve from which it derives its innervation The true cadaveric or intermediate position is half way between abduction and adduction whereas the paramedian position is somewhat nearer the midline Few observers could distinguish such a small positional difference were it not for the fact that when the crico thyroid muscle is acting there is still some cord tension and when paralysed tension is absent so that the cord presents a wavy appearance The affected cord during respiration appears shorter and lies at a slightly lower level and the cartilage of Wrisberg seems unduly prominent The reasons have already been given when discussing the effects of posticus paralysis

In a unilateral case whether the lesion is true recurrent nerve palsy or high vagus palsy there is at first inefficient closure of the glottis and a feeble husky voice results air waste on phonation is characteristic As time goes on the voice may improve because the unaffected cord compensates and swings right across the midline on phonation At first there may be some overflow of water or food into the trachea but this also improves as time goes on

When complete paralysis is bilateral there can be no hope of efficient glottic closure The voice is feeble and breathy whilst spilling over into the trachea is a constant source of worry Breathlessness is usually only evident on exertion Bilateral complete paralysis is fortunately very rare

Diagnosis —The diagnosis is almost entirely a matter of accurate inspection Obliquity of the laryngoscopic image due to faulty position of the mirror may cause confusion In nervous subjects the cords are sometimes adducted on inspiration but they will abduct naturally during the involuntary inspiration which follows a prolonged phonation The only condition which really imitates paralysis is the fixation of the arytenoid cartilage which results from disease in or around the joint its complete immobility with the presence of swelling or scarring often aids the diagnosis but in old standing cases of paralysis secondary fixation frequently occurs In cases of arytenoid fixation there is no dropping forward of the cartilage of Wrisberg

Ætiology —The movements of the cords are represented bilaterally in the cortex cerebri and stimulation of either centre produces movement (adduction) of both cords from which it follows that no unilateral lesion above the bulbar nuclei can paralyse the larynx and clinically we find that it is never affected in cases of hemiplegia The bulbar centres lie in the floor of the fourth ventricle and here a lesion of one centre causes paralysis of the cord on the same side which in a gradually progressive lesion affects first the abductor muscle Thence the nerve fibres pass in the roots of the bulbar accessory to the vagus and recurrent laryngeal nerve the cause of the paralysis may therefore be situated (1) in the medulla (2) at the base of the skull (3) in the vagus or (4) in the recurrent laryngeal nerve

Paralyses of bulbar origin are often but by no means always bilateral In lesions here and at the base of the skull neighbouring nerves are liable to be involved thus paralysis of a cord and of the palate on the same side may coexist (syndrome of Avellis) or paralysis of cord palate trapezius and sternomastoid from involvement of the

spinal accessory roots or persistent tachycardia due to damage of the cardio inhibitory centre or nerves Tabes dorsalis is the most frequent cause of paralysis of central origin it may effect one or both cords and may be associated with anæsthesia paræsthesia or the spasmodic attacks called laryngeal crises In general paralysis of the insane laryngeal palsy is not uncommon It is the rule in bulbar paralysis and is usually bilateral, but appears late in the disease Syphilitic nuclear disease pachymeningitis and gummata at the base of the brain are now rare causes, and here the ocular muscles especially the external rectus, are often attacked

Peripheral causes usually act by compression of the recurrent nerve the most frequent being aneurysm enlarged glands, tuberculous or malignant, and cancer of the œsophagus Other causes are thyroid tumours, usually but not necessarily malignant, mediastinal tumours cancer of the lung pleurisy and pulmonary tuberculosis in which the nerve, usually the right, may be involved in a lesion at the apex of the lung or by tuberculous bronchial or tracheal glands Neuritis is a cause of laryngeal paralysis, it may be produced by the toxins of diphtheria or by organic poisons, especially lead and more rarely arsenic and alcohol Finally, the condition is not uncommonly the result of trauma more especially surgical operations on the thyroid gland and lung

Prognosis —Paralysis of one cord is not in itself dangerous to life, but when the cause is undiscovered the prognosis must be guarded, for this paralysis may be for a long time the only sign of serious disease, on the other hand, the recurrent laryngeal nerve may be involved in some non-progressive lesion such as a fibrotic bronchial gland and such cases have been under observation for 20 or 30 years without change

Treatment —This depends on the cause In most cases it is but a symptom of disease elsewhere and does not call for special treatment In cases due to neuritis strychnine and the local application of the faradic current by means of an intra laryngeal electrode are indicated Tracheotomy is advisable in bilateral abductor paralysis A specially designed tube in which a valve is incorporated is used, this valve allows air to enter freely on inspiration but closes during expiration so that the voice remains unaffected Operations devised to fix one arytenoid cartilage and vocal cord in a more lateral position sometimes give satisfactory results

All patients suffering from laryngeal paralysis must be forbidden to swim

FUNCTIONAL PARALYSIS (FUNCTIONAL APHONIA)

Ætiology —Functional aphonia is a common manifestation of hysteria and occurs chiefly in young women Many cases were encountered amongst men during the War of 1914–1918 and the War of 1939–1945 men whose terrifying experiences had driven them into a state of battle exhaustion Anæmia debility and local inflammatory conditions may predispose to an attack of aphonia but it seems clear that the condition would not materialise without some hysterical background It is true that some women are rendered aphonic by acute laryngitis of moderate severity but it is not the inflammatory process which prohibits cord approximation

Symptoms —Paralysis of the adductors presents a totally different clinical picture from organic paralysis It is always bilateral the larynx appears normal while at rest but on attempts at phonation it is seen that the cords do not adduct into the position necessary for the production of the voice Occasionally the internal tensors alone are working inefficiently an elliptical chink is left between the cords anteriorly If the crico arytenoidei laterales are paretic the entire glottis remains open to a variable extent and, very rarely the arytenoideus is affected alone when a triangular aperture is left behind the vocal processes The paralysis is hardly ever complete, indeed a considerable amount of movement is usually seen though insufficient to produce phonation In purely hysterical cases onset and recovery are sudden and

the voice when regained is clear though perhaps at first less powerful than usual Whilst examining the larynx through a mirror it is well to ask the patient to cough if the cords remain separated during attempted phonation and come together on coughing the diagnosis of functional aphonia is not in doubt

When a patient assailed by some great emotional disturbance is ' struck dumb ', she is not even able to whisper for the whole speech mechanism is paralysed This is called hysterical mutism

Treatment—In patients suffering from debility the cause should be found and treated Predisposing local inflammatory conditions should be sought for and appro priately treated It is well to remember that patients suffering from chronic phthisis sometimes speak very softly and may become almost aphonic

Although in some cases of true functional aphonia the voice can be temporarily restored by powerful local stimulation this form of treatment is not recommended for aphonia will usually recur The most difficult patients to treat are those who have been unsuccessfully subjected to such local treatment.

The physician must be sympathetic yet firm and confident and it is his first duty to explain that there is no serious disease The patient may be told that the trouble results from muscular inco-ordination

The best long term results are obtained when the voice can be restored during the first interview and it is imperative that no relation or friend should be in the room A good plan is to suggest that one group of muscles in the larynx is in spasm and that without complete body relaxation it is difficult to break down this spasm The patient may be asked to lie on a comfortable couch and told to relax as though about to go to sleep It is surprising how many patients will in fact go straight into a semi hypnotic state The laryngeal box may be moved from side to side across the vertebral column and suggestions made that by breaking down the spasm in this way the voice will be fully restored More often than not when told to rouse herself and recite God Save the Queen the patient will do so in a normal voice Should the voice be not fully restored the physician must retain his attitude of complete confidence and assure his patient that there has been encouraging improvement, and that restora tion of normal function can and will be attained in a short space of time When the voice is restored it should be freely exercised Really difficult cases must be referred to an expert for psychiatric treatment.

SPASMODIC AFFECTIONS

SPASM OF THE GLOTTIS

Spasm of the laryngeal muscles produces adduction of the cords for though the abductors are probably affected they are overpowered by the stronger adductor muscles

Ætiology—(1) In the majority of cases the spasm is a reflex set up by local irritation foreign bodies including the laryngoscopic mirror irritating gases and inflammation ulceration or tumours in or near the larynx (2) Spasm is also caused by irritation of the recurrent laryngeal nerves by mediastinal tumours and especially by aneurysm (3) Central nervous lesions especially tabes (4) Functional disturbances frequently hysterical and sometimes excited by sexual disturbances

Symptoms—The attacks vary much in different subjects in severity and duration The patient clutches some support or rushes to the window The respirations are rapid and shallow with loud inspiratory stridor and in the height of a severe attack, are completely arrested with all the signs of asphyxia The subjective sensations include a horrible feeling of anxiety but consciousness is not lost Many cases are less acute but persist longer even for several hours

Prognosis—The attacks are practically never fatal, unless a foreign body or tumour be present

Treatment—During the attack amyl nitrite or chloroform may be inhaled and ampoules of these drugs should be kept at hand Between the attacks sources of irritation should be sought for and removed, the upper air passages brought to a healthy condition and the general health and mode of life should receive attention Administration of bromides may be required when the attacks recur frequently

W I DAGGETT

DISEASES OF THE TRACHEA

INFLAMMATION OR TRACHEITIS

ACUTE TRACHEITIS

Acute tracheitis may occur from any condition leading to irritation of the mucous membrane of the trachea When it occurs as a result of bacterial or chemical agency the whole of the upper air passages are usually involved in greater or less degree, and the clinical manifestations are not confined to the trachea In some cases however, the stress of the resultant reaction falls upon this tube, and the condition therefore requires separate consideration

Ætiology—1 *Microbic invasion*—This is the commonest cause The bacteria usually found associated with tracheitis are the so called catarrhal organisms such as *Neisseria catarrhalis* the pneumococcus the Friedlander pneumo bacillus and *Hæmophilus influenzæ* It is probable that the primary organism in many cases is a virus Frequently a streptococcus may be found, either alone or in association with one or more of those just mentioned As with catarrhal inflammation of other parts of the upper air-passages damp, cold or foggy climatic conditions predispose to tracheitis It is more common in young and middle aged adults than in infancy or in old age Mouth breathers are more liable to this condition Exposure to sudden changes of temperature may be a factor in its onset

Tracheitis may also occur as part of the clinical picture in some of the acute specific diseases such as enteric fever, diphtheria whooping cough and measles It is often a troublesome and distressing association or sequel of true influenza

2 *Chemical agencies*—Irritating or poisonous fumes and vapours may lead to a very acute form of tracheitis It may therefore occur in certain occupations unless adequate precautions are taken The use of poison gases in warfare has drawn widespread attention to this form of the condition since tracheitis was an almost constant result of certain forms of gassing The chief chemical irritants used in the War of 1914–1918 were chlorine phosgene and dichlordiethyl sulphide commonly known as mustard gas Of these the last was perhaps the most irritant to the trachea and fatal cases invariably showed tracheal lesions Direct inhalation of steam may also induce an acute tracheitis

3 *Mechanical causes*—The presence of a foreign body or the invasion of the trachea by extension from malignant growth in adjacent structures may lead to a local or even to a general tracheitis It is noteworthy however that the trachea is frequently spared in occupations involving the respiration of dusty air which leads to deposits in the lungs and bronchial glands with resulting pneumoconioses Although a coal miner s lungs are black yet his trachea may be practically normal

Pathology—The changes found in the trachea vary from simple catarrhal inflammation to intense destructive changes with ulceration and in some cases croupous

or membranous exudate In the catarrhal forms, the mucous membrane shows changes similar to those in bronchitis It is at first swollen red and dry the vessels running across the trachea being engorged and clearly visible Then owing to increased activity of the mucous glands excessive mucoid secretion occurs and the mucous membrane becomes moist, after which resolution may take place or the process may proceed to a muco purulent stage when the fluid on the membrane coheres to form yellowish or green tenacious pellets Occasionally numerous red blood cells are extruded and the tracheal exudate becomes streaked tinged or uniformly pinkish

In some inflammations such as those induced by poison gases or inhaled steam the mucous membrane may be intensely engorged and actual destruction may occur involving even the deeper structures and the cartilages so that greyish yellow sloughs result which on separation leave ulcers In diphtheria the characteristic false membrane composed of necrosing fibrin leucocytes and bacilli may be found loosely attached to the mucous membrane as in other localisations of this process It may be primary or secondary to faucial or laryngeal diphtheria either by direct extension or through diphtheritic infection of a tracheotomy wound

In influenza the pink appearance of the trachea is of such constancy in fatal cases that it has come to be regarded as one of the most characteristic post mortem changes found in this disease The bright injection generally involves the lower half of the trachea but it may occur along the whole length of this tube

In whooping cough the inflammatory reaction is usually less acute

In typhoid fever small ulcers may occasionally be found in the trachea similar to those occurring more commonly in the larynx

Symptoms —Acute catarrhal tracheitis usually begins more or less acutely like the common cold of which it is to be regarded as one form with malaise slight headache and a mild degree of fever the temperature being usually between 99 and 100 F rarely 101 F The patient soon experiences a sensation of irritation behind the sternum rapidly leading to a harsh dry cough of noisy character The cough aggravates the retrosternal discomfort which develops into a sensation of rawness or soreness making the cough very painful and distressing If the larynx is involved at the same time the voice becomes hoarse and sometimes lost or reduced to a raucous whisper In tracheitis alone the voice is usually unaffected After from 12 to 24 hours the condition passes into the mucoid stage The cough becomes looser and less painful and small pellets of tenacious mucus are coughed up usually greyish or black in town dwellers whitish in those in rural conditions in either case the mucus may be streaked with blood or even tinged a uniform pink colour in the more acute forms it sometimes becomes yellow and more purulent In the mucoid stage the retrosternal soreness becomes less the constitutional symptoms abate while the temperature subsides and becomes subnormal The patient often feels weak and out of health for some days and is sometimes left with a noisy morning cough and tracheal irritation which may last for days or weeks The aspect of the patient shows nothing characteristic There is the general appearance of fever malaise and discomfort The rise of temperature and increase in pulse rate are usually moderate In the early stages physical examination of the chest shows no abnormality but when exudation occurs a coarse wheeze may be audible over the trachea particularly when the patient takes a deep breath or just before a cough occurs

Diagnosis —The association of catarrhal symptoms with a dry harsh cough and retrosternal soreness without signs of bronchitis is almost pathognomonic In some cases the diagnosis can be established with the laryngoscope or by endoscopy but in most the discomfort which these examinations entail is unnecessary

Prognosis —This is almost invariably good except in debilitated subjects or in those with cardiac or renal disease, in whom the process may spread to the larynx

bronchi or lungs The usual course is from 2 days to a week though cough and expectoration may persist for days or weeks The condition may become chronic To some extent the prognosis depends upon the care and treatment in the initial stage Cases that are neglected are liable to become chronic

Treatment —The prophylactic and remedial treatments of acute tracheitis are practically identical with that of acute bronchitis of the larger tubes Even in mild cases the patient should go to bed though this may be necessary only for 1 or 2 days but he should keep to his room till his temperature has become normal There may be less need for expectorants than in bronchitis, and a simple saline diaphoretic mixture with the addition later of tinct ipecac and tinct opii camphorata may be all that is necessary Sedative inhalations such as vapor benzoini are useful, and counter irritation to the sternal region is comforting to the patient When a chronic noisy cough develops a mixture containing small doses of apomorphine and tinct chloroform et morphin co often gives relief or codeine linctus B P C Penicillin is often of value given by inhalation or in severe cases by injection (pp 8 and 9)

When tracheitis occurs as part of some specific disease such as diphtheria or influenza the treatment should be that appropriate to the primary disease

In gassing ' every effort should be made to relieve the distressing and painful symptoms and for this purpose morphine may be required Various inhalations may be tried, and useless cough should be checked by sedative mixtures or by a linctus of heroin, morphine or codeine

CHRONIC TRACHEITIS

Ætiology —Chronic tracheitis may follow an acute attack, or it may develop insidiously in patients suffering from chronic laryngitis or bronchitis Inhalation of cigarette smoke is a not infrequent cause It is also sometimes a sequel of chronic rhinitis especially of the atrophic form or ozœna A certain degree of chronic tracheitis accompanies the specific lesions of syphilis and tuberculosis, which are described below

Pathology —Various degrees of chronic inflammatory lesions may be found In chronic catarrhal tracheitis the vessels are distended or engorged and the mucous membrane of the trachea becomes thickened and more or less covered with mucoid or muco purulent secretion the histological changes being those of chronic catarrhal inflammation namely shedding of the ciliated epithelial cells overactivity of the mucous glands and sometimes thickening and induration of the submucous tissues from proliferative changes A condition of perichondritis of the tracheal cartilages may, in this case, be observed and this may result in a mammillated appearance in the internal aspect of the trachea In ozœna, crusts similar to those in the nose and pharynx may form on the tracheal mucosa

Symptoms —The symptoms of chronic tracheitis are similar to those of the acute form There is a sense of discomfort and irritation about the trachea and a chronic almost dry cough often worse in the morning There is generally some scanty sticky expectoration mucoid or muco purulent, darkened by carbon particles and occasionally blood tinged

There are practically no physical signs of this condition except that the tracheal changes can be observed by the laryngoscope or by endoscopy of the trachea

Diagnosis —This is concerned chiefly with its differentiation from chronic changes in the trachea due to syphilis tuberculosis or leprosy and confirmation that it is not caused by the presence of new growth It must largely be made by endoscopic examination

Prognosis —The prognosis depends upon the cause When this can be removed as by treatment of predisposing conditions in the nose and throat, the outlook is good

When the tracheitis is due to other conditions such as syphilis and tuberculosis it depends upon the situation and extent of the other lesions and upon the treatment adopted

Treatment—This is in its main features similar to that of acute tracheitis but climatic treatment may be of great importance The patient may perhaps spend the winter months in a warm or equable and clear climate with great advantage When other conditions are concerned such as ozœna, syphilis or tuberculosis the treatment appropriate to them should be employed as well

CYSTS AND TUMOURS

These are rare conditions but require careful consideration

CYSTS

Owing to weakening of the wall of the trachea local bulging may occur giving rise to a cystic air containing swelling in the neck in direct communication with the lumen of the trachea Such cysts are known as tracheoceles or aeroceles They are resonant to percussion and can often be temporarily reduced by pressure

Small retention cysts may occur in the posterior wall of the trachea from obstruction of the ducts of the mucous glands as they pass through the trachealis muscle They are of pathological interest only and do not give rise to symptoms

SIMPLE TUMOURS

The most important is papilloma It occurs chiefly in children and is usually pedunculated When it grows in polypoid form it may lead to obstruction of the trachea low down in which case tracheotomy may fail to give relief and death results unless the tumour can be removed by endoscopic methods

Other innocent tumours occur but are rare They include enchondrosis from localised overgrowth of cartilage multiple enchondromata and osteoma from ossification of a pre existing enchondroma Lipoma and aberrant thyroid tumours may occur, but are very rare

Symptoms—These tumours produce varying degrees of tracheal obstruction and can usually only be recognised by endoscopy Treatment is considered under that of tracheal obstruction

MALIGNANT TUMOURS

A few cases of primary carcinoma of the trachea have been recorded Secondary growths are not common but the trachea is often involved and infiltrated by primary carcinoma in adjacent structures such as the œsophagus the bronchus the thyroid the larynx or by the extension of secondary deposits in the cervical or mediastinal glands

Primary sarcoma of the trachea is also very rare The growth is usually smooth and not pedunculated Secondary deposits of sarcoma in the trachea may occur from sarcoma of distant organs such as the kidney or it may be invaded directly by sarcoma originating in the thymus or other mediastinal structures and especially by lympho sarcoma of the mediastinal glands

Symptoms—The tracheal symptoms and signs are usually those of obstruction accompanied by pain When the primary growth is in the œsophagus antecedent

dysphagia and sometimes laryngeal paralysis reveal the origin of the tracheal symptoms when they occur In this case copious frothy mucoid expectoration is frequent, and when ulceration develops with perforation, food particles may enter the trachea excite cough and soon lead to inhalation broncho pneumonia or gangrene When the growth is near the bifurcation urgent dyspnœa is the rule, and spasmodic attacks may occur causing extreme distress In most cases of tracheal growth the characteristic clanging brassy cough (gander cough) of tracheal obstruction can be heard The trachea may be pushed to one side and its lumen distorted and obstructed by growth in the cervical glands or in the thyroid gland In mediastinal new growth invading the trachea, the pressure signs and symptoms characteristic of that disease usually render the explanation of the tracheal symptoms apparent

Diagnosis —Intratracheal growths have to be differentiated from other causes of tracheal obstruction, and the diagnosis is considered in detail under that condition Endoscopy affords valuable confirmation if it is practicable or desirable In œsophageal and mediastinal new-growths invading the trachea, radiographic examination may assist in diagnosis

Course —This is generally rapidly progressive

Prognosis —This is hopeless death occurring from asphyxia or from some complication or by asthenia

Treatment —Treatment can be palliative and symptomatic only In obstruction it may be possible in rare cases to give temporary relief by a low tracheotomy but, as a rule, this is impossible, owing to the presence of obstruction below any point where the trachea is accessible

THE INFECTIVE GRANULOMATA

SYPHILIS

The trachea may be affected in both the congenital and acquired forms

In congenital syphilis a progressive cicatrisation may occur leading to stenosis In acquired syphilis during the secondary stage the mucous membrane of the trachea may become generally hyperæmic or small raised mucous patches may develop locally In the tertiary period gummata may occur in the trachea, the commonest site being towards the lower end Degenerative processes leading to necrosis and softening eventually result in ulceration sometimes with local sloughing of parts of the tracheal rings In the process of cicatrisation a progressive stenosis may develop

Symptoms —Symptoms are those of chronic tracheitis and tracheal irritation in both the secondary and tertiary manifestations but in the latter, signs of tracheal stenosis may develop when scarring and healing are in progress Laryngeal involvement occurring at the same time tends to distract attention from the tracheal lesions or to obscure them

Diagnosis —The diagnosis of syphilis of the trachea depends upon a careful study of the history of the case indications of tracheal irritation laryngoscopic or endoscopic examination, the coexistence of other manifestations of syphilis and in their absence a positive Wassermann reaction

Prognosis —If the condition is recognised early excellent results may be obtained by treatment but it is obvious that where deep destructive changes have resulted, medicinal measures can only palliate

Treatment —Antisyphilitic treatment should be administered vigorously In cases of stenosis of the trachea from cicatrisation dilatation of the stricture by means of bougies introduced through an endoscope may be practicable and afford useful help

TUBERCULOSIS

Tuberculosis of the trachea may be found post mortem in advanced cases of pulmonary tuberculosis usually in those with extensive laryngeal involvement Primary tracheal tuberculosis is unknown Secondary lesions in the trachea and bronchi are found not infrequently on systematic endoscopic examination

Pathology —Tuberculous lesions may occur at any part of the trachea but they are more frequent in the lower part and on the posterior wall When they occur they are usually numerous There may be some general hyperæmia or small tubercles varying in size from a pin s head to a split pea may be visible Later superficial ulceration occurs forming irregular punched out ulcers Occasionally the process may extend deeper and erosion of the cartilages may occur with the formation of sinuses and even fistulous communication with the œsophagus

Symptoms —Since tracheal tuberculosis is usually a late manifestation of advanced disease its clinical indications are slight and are usually obscured by the more obvious laryngeal and pulmonary symptoms and signs though if the process extends deeply and produces sinuses and fistulous tracks it may become apparent The actual tracheal symptoms are those of cough and retrosternal soreness

Diagnosis —This condition has to be distinguished from other chronic tracheal lesions and a diagnosis can only be made from a careful review of the history the general evidence of tuberculous disease and by the tracheal involvement which may be visible by endoscopy

Treatment —American observers have treated the lesions by cauterisation with silver nitrate Streptomycin and isoniazid are usually effective

LEPROSY

In some cases of this disease, granulomatous lesions occur in the trachea and these may eventually give rise to tracheal stenosis owing to the contraction of new formed fibrous tissue The diagnosis can only be made from the occurrence of tracheal symptoms in a case with established lesions of leprosy in other parts

The treatment is symptomatic

SCLEROMA

Although in most cases this condition affects the nose only scleromatous lesions may be found in the trachea as a pathological curiosity The disease in any form is rare in England and occurs chiefly in Poland and Austria The nodules of granulomatous tissue in the trachea may cause partial obstruction mechanically or on contraction lead to actual stenosis

TRACHEAL OBSTRUCTION

Obstruction to the lumen of the trachea may be produced by foreign bodies by conditions originating in the trachea and by pressure from without

FOREIGN BODIES IN THE TRACHEA

The commonest route by which foreign bodies enter the trachea is through the mouth and larynx in the acts of breathing laughing yawning sighing or before and after coughing when food or some foreign substance is in the mouth A piece of bone a stud button false teeth chewing gum peas articles of food nuts grains of wheat, beads or blades of grass are among the substances which may gain entrance

to the trachea in this manner Surgical operations in the mouth and throat may lead to the inhalation of a tooth a piece of tonsil or a mass of adenoid tissue Material vomited from the stomach, such as food, blood clot or intestinal worms may be inhaled into the trachea A large blood clot in hæmoptysis may temporarily obstruct it Foreign bodies such as small projectiles embedded in old wounds of the neck peices of new growth or tuberculous glands may also gain access by ulceration through the tracheal wall

Unless it becomes impacted, or is too large to enter one of the two main bronchi a foreign body rarely remains long in the trachea It either causes death with dramatic rapidity is coughed out again, or passes down into one or other of the large bronchi or their secondary divisions, where it produces results which are described in the section on diseases of the bronchi

Symptoms —These depend upon the mode of entry the size of the foreign body, and the degree of obstruction to the air current which it induces but in general the tracheal symptoms are less urgent than those of laryngeal obstruction and less serious than those of obstruction of one or other main bronchus There may be intense dyspnœa with great discomfort and alarm during the actual passage through the larynx of a small foreign body especially if it is temporarily arrested there but when it enters the trachea there is an almost instantaneous cessation of the acute distress though some degree of dyspnœa may persist The type of dyspnœa is inspiratory in the main though a minor degree of expiratory difficulty may be apparent if the foreign body is of considerable size There may be a definite stridor with both phases of respiration, but it is more pronounced in inspiration If the foreign body remains loose in the trachea which may occur if it is rounded and too large to engage in one of the main bronchial divisions a sound of vibratory character may be heard on auscultation of the trachea sometimes described as the *bruit de grelottement* This may be produced by friction of the foreign body against the tracheal wall or more commonly by the air passing over it during respiration A paroxysmal cough may occur caused by the foreign body irritating the sensitive posterior wall of the trachea and during such an attack the foreign body may be forced up to the larynx obstruct it or cause reflex spasm with intense dyspnœa and cyanosis and a risk of suffocation unless it drops back is coughed out or removed When sudden rupture of caseous material into the trachea occurs the lumen may be blocked and death take place rapidly

Diagnosis —The history of disappearance of some object from the mouth during coughing breathing or laughing should give rise to suspicion of an inhaled foreign body and this may be confirmed by seeing the object directly by endoscopy or indirectly by means of the radiograph

Course —A foreign body impacted in the trachea may give rise to septic inflammation of its walls with subsequent cicatrisation after removal or it may lead to secondary infective processes in the lungs such as purulent bronchitis and bronchopneumonia

Prognosis —This depends in the main on the nature of the foreign body and the time elapsing before its removal An irregular rough or soft foreign body is more likely to induce septic complications than a smooth hard substance Apart from rapidly fatal results the prognosis is better with intratracheal foreign bodies than with those reaching the bronchi If removal is effected within 24 to 36 hours recovery is usually rapid and complete

Treatment —Treatment consists in rapid removal with as little damage to the trachea and larynx as possible This may be effected by means of forceps passed through a bronchoscope or rarely by tracheotomy alone when the foreign body may be coughed out through the opening or be easily removed by forceps Inversion of the patient in the hope that gravity may assist the expiratory efforts of cough is dangerous and should only be attempted after tracheotomy has been performed Where

rupture of a caseous gland or softening new growth occurs into the trachea an *immediate tracheotomy may be necessary*

OBSTRUCTION FROM CICATRISATION OF THE TRACHEAL WALLS

Ætiology —This may result from any condition leading to ulceration of the *tracheal walls with subsequent healing such as a syphilitic gumma or less commonly* other granulomata such as tubercle leprosy or scleroma Another cause is cicatrisation from wounds of the trachea accidental suicidal or after tracheotomy when the incision has been made too near the cricoid or when the wound has become infected or the tube left in too long Scarring from damage to the trachea by the inhalation of boiling or caustic liquids or even by inhaled gases may lead to stenosis

Pathology —The deformity of the trachea and the obstruction of its lumen depend upon the situation and the extent of the cicatricial contraction of its walls It may be local producing an hour glass constriction or involve a long extent of the tube Occasionally especially in syphilitic lesions stenosis may occur at two different levels

Symptoms —These depend upon the degree of stenosis the rapidity with which it develops and the condition of the larynx bronchi and lungs When the stenosis is produced gradually as in cicatrisation a degree of obstruction may result greater than would be compatible with life if suddenly induced In the early stages of a progressive stenosis slight dyspnœa may be present on exertion and during sleep a faint stridor may be audible disappearing when the patient is awake As the contraction progresses the dyspnœa becomes more marked and a definite and persistent stridor develops at first inspiratory only though expiration may become both noisy and obstructed The patient may experience a sensation of obstruction referred to the neck or under the sternum accompanied by pain and irritation leading to cough which may be dry noisy and metallic or accompanied by more or less frothy sputum if the primary condition is associated with widespread tracheitis The voice may lose tone and volume and the patient talk more quietly than normal and with some evident effort In advancing stenosis sudden and alarming attacks of dyspnœa may occur leading to cyanosis and threatening suffocation These attacks are usually due to an accumulation of mucus at the site of the stenosis The patient in advancing degrees of obstruction cannot lie down and generally sits leaning forward with chin depressed It may be noted that the extraordinary muscles of respiration contract forcibly and yet the laryngeal excursions may be small or hardly noticeable in contrast with those of laryngeal obstruction in which they are maximal This distinguishing sign was first pointed out by Gerhardt and is of value but unfortunately it is not absolute and cannot therefore be regarded as pathognomonic On auscultation over the trachea a noisy roar may be audible of maximum intensity near to the obstruction whereas the breath sounds over both lungs may be deficient although the stridor may be conducted bilaterally

Diagnosis —Tracheal obstruction from cicatrisation has to be distinguished from laryngeal obstruction in which the symptoms are usually more acute and more urgent Gerhardt s sign described above may also be suggestive It has also to be differentiated from obstruction due to pressure from without (*vide infra*) The only reliable method of distinction is by direct inspection with the bronchoscope

Course —The course of cicatricial stenosis is usually progressive unless arrested by treatment and the dyspnœic attacks become more frequent and alarming

Prognosis —Early syphilitic stenosis may be arrested by appropriate antisyphilitic treatment Obstruction due to other granulomatous conditions varies with the severity and extent of the primary lesions Caseous material or degenerated growth ulcerating

into the trachea is usually immediately fatal or leads to death within a few days from pulmonary complications

Treatment—*Rest should be advised with avoidance of exertion, smoking and alcohol* The patient's fears should be allayed and symptomatic treatment ordered such as sedative inhalations or a linctus to check useless cough In syphilitic stenosis vigorous antisyphilitic treatment should be given A low tracheotomy may be necessary for an intractable stricture high up in the trachea In some cases where an ordinary tracheotomy cannot be performed below the stricture it may be possible to insert Koenig's long tracheotomy tube through an opening in the trachea made above it In other cases dilatation of a fibrous stricture by bougies passed through an endoscope may be feasible

OBSTRUCTION FROM EXTERNAL PRESSURE

Pressure on the trachea may occur in the neck or in the mediastinum

Causes of pressure in the neck—Strangulation, throttling and garotting lead to death by occlusion of the trachea and suffocation *Enlargement of both lobes of the* thyroid body may cause lateral compression of the trachea, until eventually its lumen is reduced to a narrow slit—the so called 'scabbard trachea' Irregular or unilateral enlargements on the other hand cause deviation of the trachea with kinking of its lumen Other less common causes of compression of the trachea are enlargement of the cervical glands from tuberculosis malignant disease *Hodgkin's disease or leukæmia* The trachea may be pressed on from behind by a foreign body impacted in the œsophagus or by a bony tumour arising from the vertebræ

Causes of pressure in the mediastinum—An aneurysm of the aortic arch may press directly upon the trachea at or near the bifurcation and cause obstruction Similarly deep pressure may be caused by a retrosternal goitre a persistent and enlarged thymus, or a thymic abscess mediastinal glands enlarged from any cause, usually malignant disease, a dermoid cyst or a bony tumour originating in the sternum

Symptoms—The symptoms are in the main identical with those of stenosis of the *trachea from intrinsic causes with the special symptoms due to the primary* external condition superadded

Diagnosis—This may be simple and obvious, as in those cases due to pressure from tumours in the neck whereas in those due to mediastinal pressure it is usually only possible after a careful survey of all the symptoms and is in brief identical with that of aneurysm or mediastinal new growth to which reference should be made In some cases radiographic examination may give valuable information

Prognosis—This is good in obstruction due to causes in the neck other than malignant disease but it is grave almost hopeless in obstruction due to mediastinal *causes with the exception of abscess, goitre,* dermoid cyst and some thymic conditions

Treatment—The treatment is that of the primary condition In goitre and tuberculous glands in simple tumours cysts and some thymic condition operation may be possible and may effect complete cure In those due to mediastinal pressure, especially from aneurysm or new growth treatment in *most cases*, can be only palliative or symptomatic and directed to the relief of pain dyspnœa cough and distress

INJURY

Direct violence to the trachea has been known to cause rupture when the chin is raised upwards and the trachea is thereby extended

R A YOUNG
G E BEAUMONT
L R BOLAND

DISEASES OF THE BRONCHI

BRONCHITIS

Inflammation of the bronchi or bronchitis is one of the commonest maladies and may be induced by a variety of causes These, in the main fall into three groups bacterial chemical and mechanical similar to the causes of tracheitis which is indeed in many cases a concomitant or antecedent of bronchitis so that tracheo bronchitis would be a more accurate designation of the majority of cases At the same time it should be recognised that the trachea may be alone or predominantly affected while on the other hand in many cases of bronchitis of the smaller tubes the trachea may escape or be only slightly involved

Bronchitis is so varied in its extent and in the form and severity of its manifestations that a satisfactory classification is somewhat difficult to formulate We propose to consider the clinical manifestations of bronchitis according to the following classification

1 Acute Forms —(*a*) Catarrhal bronchitis (1) of the larger tubes (2) of the smaller tubes (*b*) suppurative (*c*) secondary bronchitis (*d*) bronchitis due to mechanical and chemical agencies (*e*) fibrinous

2 Chronic Forms—(*a*) Catarrhal (*b*) suppurative (*c*) secondary (*d*) due to mechanical agencies and (*e*) fibrinous

1 ACUTE BRONCHITIS

ACUTE CATARRHAL BRONCHITIS OF THE LARGER TUBES

Synonyms —This condition is often called Bronchial Catarrh or Acute Tracheo bronchitis

Ætiology —*Predisposing causes* —Climate undoubtedly plays an important part Catarrhal bronchitis is rare in polar and arctic regions and near the equator but is very prevalent in damp and foggy climates In England attacks are common in late autumn winter and early spring Owing chiefly to greater exposure the disease occurs more frequently in men than in women It is most common at the extremes of life infancy and old age but it is not infrequent at any age Fatigue and privation play their part and exposure to cold wet or fog so frequently seems to initiate the attack that it is often regarded as the exciting cause Scoliosis kypho scoliosis and other malformations or deformities of the chest predispose to bronchitis and some of them are induced or aggravated by bronchitis early in life Chronic cardiac and renal disease both render their subjects more liable to bronchitis as do also conditions of the nose and pharynx which lead to mouth breathing in consequence of the inhalation of air which is unwarmed and unfiltered by the nose There is a popular idea that a child may cut its teeth with bronchitis but the combination is probably coincidental

The exciting cause is not really known There is a suspicion that the infection is primarily viral in origin Pneumococci streptococci *Neisseria catarrhalis* staphylococci *Hæmophilus influenzæ* Friedlander s bacilli (*Kl pneumoniæ*) are found in the sputum or tissues but they are probably secondary invaders

Pathology —The changes induced in the bronchi are similar to those in the nasal mucosa in coryza and in the trachea in tracheitis Three stages may be described An initial dry stage when there is active hyperæmia of the bronchial mucosa with exudation into the submucous layer causing temporary diminution of the bronchial secretion from occlusion of the mucous ducts The second or mucoid stage is associated with copious discharge of mucoid secretion owing to increased

activity of the mucous glands this secretion being mixed with shed ciliated epithelial cells and scanty leucocytes Sometimes in acute cases a few red blood corpuscles are present The third stage is that of resolution though not infrequently a muco purulent stage occurs when the sputum becomes less copious and greenish in colour from large numbers of pus cells

In fatal cases the lung tissue may appear slightly distended and red while the bases may be sodden from œdema On section the bronchi appear injected and the mucosa is swollen On squeezing the lung beads of mucoid fluid or muco pus exude from the cut ends of the bronchi There is no consolidation and the lung tissue floats in water

Symptoms —An attack of acute bronchitis generally begins suddenly with *malaise, aching in the limbs and a sense of oppression in the chest* If the trachea is also involved, there is the characteristic feeling of rawness under the sternum The temperature rises, varying from 99° to 100° F in mild cases to 103° F in more severe ones The cough is at first dry irritating and ineffective but in a few hours it becomes looser The sputum in the early stage is scanty, tenacious and sometimes streaked with blood, it then becomes copious, mucoid and frothy in character, and is found to contain mucus, shed epithelial cells leucocytes and red blood corpuscles Later it lessens in quantity and may become thick yellow and muco purulent With the onset of expectoration there is generally an abatement in the symptoms the rawness under the sternum disappears and the feeling of pain or soreness about the pectoral muscles and the costal attachments of the diaphragm lessens The febrile reaction may last only 3 or 4 days but the cough and expectoration may go on for 10 days or longer gradually diminishing until they are present only night and morning and then cease completely

In the early stage the patient is flushed and the breathing may be slightly in creased in rate but it is rarely or never laboured unless emphysema coexists Vocal fremitus is unaltered but rhonchal fremitus may sometimes be felt over one lung or both The chief physical signs are discovered only on auscultation The breath sounds may be harsher and higher pitched particularly in infants and children but they remain vesicular and expiration may be prolonged The voice conduction is unaltered As a rule rhonchi either sonorous or sibilant according to the size of the bronchus in which they are produced are audible over both lungs, and during the mucoid stage bubbling rales may be heard especially at the bases

Complications and Sequelæ —Bronchitis may go on to broncho pneumonia lobar pneumonia aspiration pneumonia lobular atelectasis fibroid induration or bronchiectasis It may lead to chronic bronchitis or be followed by active tuber culosis Occasionally acute interstitial emphysema may result from violent coughing

Diagnosis —The diagnosis of bronchitis is usually easy owing to the character istic rhonchi but it is important to differentiate primary bronchitis from bronchitis *occurring as a secondary condition in acute specific fevers* and other diseases

Course —This is variable The patient may be convalescent in from 7 to 14 days but cough expectoration and a condition of debility may continue for several weeks though in this case the possibility of pulmonary tuberculosis should always be considered

Prognosis —Bronchitis of the larger tubes is rarely fatal except when it occurs in infants or the aged or as a complication of advanced cardiac or renal disease

Treatment —PROPHYLACTIC —This consists in the avoidance of stuffy ill venti lated rooms and places of entertainment when catarrhal infections are rife In mouth breathers, steps should be taken to deal with the conditions of the naso pharynx inducing this habit and instruction in normal breathing given In dusty occupa tions suitable measures should be taken to minimise the irritant particles in the air as is now done in most factories and workshops Where poisonous gases have to be encountered some form of efficient gas mask should be utilised

Vaccines have been and still are widely used in the prophylactic treatment of catarrhal infections They have their enthusiastic adherents amongst doctors and patients but there is no objective evidence of their efficiency and much to the contrary

CURATIVE —No matter how mild the attack may be at the onset the patient should be kept in bed This may only be necessary for 1 or 2 days but he should keep to his room till his temperature has returned to normal The room temperature should be kept at 60 to 65° F While the temperature is raised the diet should be simple adapted to the patient s appetite and the febrile condition The patient should take plenty of fluids and hot warm drinks are often welcome The air of the bedroom may be moistened by the use of a steam kettle in the dry stage but steam tents should not be used Hot compresses over the sternum sometimes help to relieve the raw soreness The inhalation of steam is comforting and vapor benzoini—60 minims to the pint of water at 160 F or vapor pini 120 minims to the pint—is often added to the water During the dry and painful period of acute bronchitis a sedative linctus may ge given Once expectoration starts mixtures containing ammonium chloride or carbonate combined with squills and flavoured with syrup of tolu or of Virginian prune may be given Sedatives may be necessary at night—Dover s powder gr 10 with or without aspirin barbitone gr 5 to 10 or chloral hydrate gr 10 to 20 are all suitable Opium and its derivatives are best avoided Antibiotics are not usually necessary or required although they may cut down the secondary infection and are often given as a routine to elderly patients The older the patient the longer should be the convalescence Premature return to normal life may be followed by a relapse or perpetuation of the bronchitis for weeks

When bronchitis occurs as a part of some specific disease such as diphtheria or influenza the treatment should be that appropriate to the particular disease

ACUTE CATARRHAL BRONCHITIS OF THE SMALLER TUBES

Synonym —Capillary Bronchitis

It is open to question whether this condition exists as a separate entity When the finer bronchi and bronchioles are inflamed the alveoli invariably become involved since very little swelling of the bronchiolar walls is sufficient to occlude the lumen of the tube with the inevitable production of an area of lobular collapse The transi tion from this condition to actual lobular pneumonia is a very small one In any case the causes the symptoms and the treatment of capillary bronchitis and broncho pneumonia are identical (see Broncho pneumonia)

ACUTE SUPPURATIVE BRONCHITIS

Synonyms —Sometimes called Acute Purulent Bronchitis

This condition was brought into prominence during the War of 1914–1918 In 1916 and 1917 it appeared in epidemic form amongst the British troops in England and France Although it was then regarded by some observers as a new disease it is more probable that it was in reality an epidemic form of a condition usually rare and sporadic and previously termed suffocative catarrh

Ætiology —*Predisposing causes* —The exceptionally severe winter of 1916-1917 together with conditions of overcrowding in huts and billets were undoubtedly concerned in the epidemic just mentioned The condition affects young adults chiefly and is much more common in men Over exertion fatigue and debility predispose to it but the disease may occur in robust and healthy persons A history of chill may be given but often no obvious cause can be discovered

Exciting cause —The organisms usually found are the pneumococcus and *H influenzæ* the latter being reported in 90 per cent in some series of cases *N catarrhalis* is also sometimes present

Pathology —A very intense inflammation occurs in the medium sized and small bronchi, leading to an exudate rich in leucocytes The inflammatory process may *extend to the alveoli which then contain a fibrinous fluid, with entangled red cells* The condition occurs in both lungs and is usually almost universal no portion being spared Post mortem the lungs are heavy and red in colour On section the bronchi are found to contain a thick yellow purulent fluid Small areas of collapse and some times of broncho pneumonic consolidation are seen, and there is usually œdema of the bases Plastic pleurisy is not infrequent and the glands at the root of the lungs are enlarged

Symptoms —*The onset is usually abrupt, often in young people apparently in* robust health A definite chill may occur, or only coryza and general malaise with aching of the muscles The temperature rises quickly and may reach 104° F early in the disease A cough soon develops and extreme dyspnœa is a characteristic feature Expectoration starts early, often on the second or third day At first it may be streaked with blood but it soon becomes yellowish green and nummular it consists of almost pure pus there is often as much as 5 or 6 oz in 24 hours In most instances there is great prostration *In grave cases the patient becomes unconscious and loses* control of the sphincters

There is intense cyanosis the face lips and ears being purple The respirations are rapid, 30 or 40 per minute, and the accessory muscles are often in full action Palpation and percussion may not show any abnormality though slight dullness is sometimes present at the bases At first no signs may be discovered on auscultation, but soon the breath sounds become largely obscured by medium sized bubbling rales often audible from apex to base both front and back The pulse is frequent the right heart may dilate and the heart sounds become weak

Complications and Sequelæ —In severe cases recurrent bronchitis broncho pneumonia fibroid disease or emphysema may follow

Diagnosis —*The early occurrence of marked dyspnœa and cyanosis* the expectoration of copious pus and the widespread rales without dullness are very suggestive of acute suppurative bronchitis The disease must be differentiated from other conditions described as acute suffocative catarrh that are associated with extreme dyspnœa and cyanosis

Acute pulmonary œdema is usually afebrile and the sputum is albuminous frothy and copious The condition leading to it such as cardiac or renal disease may be apparent

Capillary bronchitis or broncho pneumonia may give rise to difficulty but in these conditions the sputum is scanty tenacious sometimes rusty and but rarely purulent, moreover cyanosis and dyspnœa develop late and depend upon the extent *of the disease and the condition of the right side of the heart*

Pneumonia of the wandering type may simulate this condition but the character of the signs with dullness and tubular breathing and the rusty sputum usually render diagnosis easy

Course —*In favourable* cases complete restoration to health results In severe cases the course is rapid the patient becomes comatose from toxæmia expectoration ceases and death occurs from exhaustion in 2 or 3 days from the onset In other cases the disease may last for 6 weeks and proceed to recovery or death

Prognosis —This is very grave The mortality is high often as much as 50 per cent Cases extending to 3 weeks or more with swinging temperatures usually recover

Treatment —The disease is highly infectious and the patients should be isolated In the 1916 1917 and 1918 epidemics death occurred earliest and most frequently in those who walked about while infected Immediate rest in bed is essential and oxygen should be given from the beginning by double nasal catheter or B L B mask Penicillin or other suitable antibiotic as indicated by the sputum should be tried from the start

SECONDARY BRONCHITIS

Ætiology—Bronchitis usually of catarrhal type—indistinguishable as regards symptoms and sign from primary acute catarrhal bronchitis—occurs as a definite part of many acute infectious diseases and as a complication in others Among these may be mentioned measles whooping cough influenza the enteric group small pox diphtheria malaria and plague Acute nephritis of infective origin is often accompanied by acute bronchitis Other conditions associated with bronchitis are pulmonary tuberculosis glanders secondary syphilis pleurisy and gunshot wounds

Diagnosis—Bronchitis is easy to recognise but it is important not to overlook the fact that it may not be the primary condition In all cases of bronchitis in the early stages the possibility of a primary acute specific infection should be borne in mind The diagnosis is also of importance in regard to treatment—for example in malaria nephritis and syphilis in which treatment directed to the primary condition may be more helpful than the ordinary treatment of catarrhal bronchitis

BRONCHITIS DUE TO MECHANICAL AND CHEMICAL AGENCIES

Ætiology—*Mechanical*—Attacks of acute bronchitis may be caused by the inhalation of dust laden air In occupations where the worker is liable to inspire fine particles of carbon silica steel iron asbestos or kaolin acute bronchitis may result but more often these conditions lead to chronic bronchitis and pneumoconiosis Some industrial dusts are especially irritating manganese dioxide and basic slag and certain fine wood dusts from West Africa are examples of these

Chemical—Acute bronchitis may follow the inhalation of chemical irritants either as a result of occupation accidents attempts at suicide or the use of poison gases in warfare Special attention has been drawn to this subject by the large number of cases of gassing dealt with in the War of 1914–1918 Death not infrequently occurred much acute suffering was caused and some permanent damage has resulted in many cases which recovered Mustard gas produces its chief effects upon the skin the eyes and the bronchi A fibrinous exudate forms on the mucosa as a false membrane which separates as a slough The suffocative gases chlorine and phosgene affect the alveoli primarily and more intensely Chlorine inhaled in a concentration of 1 in 10 000 causes a rapid alveolar flooding with a serous and highly albuminous fluid and if the victim does not die at once he is liable to suffer from an acute bronchitis A condition called bronchiolitis fibrosa obliterans may occur as a sequel It is often associated with asthmatic dyspnœa Lewisite produces much the same effect on the lungs as mustard gas The only noxious gases likely to be met with in civilian life are nitrous fumes chlorine and ammonia

Symptoms—These are similar to those of acute catarrhal bronchitis but there is great pain distress and almost constant cough often with copious expectoration

The treatment is referred to under the heading of Tracheitis and is in the main symptomatic and directed to the relief of pain useless cough and distress If there is cyanosis oxygen should be given continuously if necessary by double nasal catheter B L B mask or oxygen tent

ACUTE FIBRINOUS BRONCHITIS

Synonym—Acute Plastic Bronchitis

Definition—A comparatively rare acute disease in which there is inflammation of the bronchi with the formation of casts These may be hollow or solid and are coughed up in the expectoration

There are some who deny that this is a disease *sui generis* and who maintain that it is but a condition found occasionally in bronchitis It appears to have been known to the ancients and in more recent times was well described by Osler and McCrae and more recently by Davidson Both these accounts describe it as a separate entity

Ætiology—It is more common in males and is met with both in children and

in adults It may begin as a primary catarrhal bronchitis or develop as a complication of enteric fever, measles or pulmonary tuberculosis Such organisms as the pneumococcus or a streptococcus may be found in the casts

Pathology —The casts may involve the main bronchi only, or more frequently the smaller ones and the bronchioles They are greyish white solid or tubular and when large, bear the impress upon their exterior of the bronchial walls in which they have been enclosed Thus when a cast extends up to the lower portion of the trachea, the indentations made by the tracheal rings may be seen impressed upon it The fine terminations generally show a spiral moulding Chemically they consist of fibrin or of fibrin and mucin Post mortem the casts may be seen in some places *in situ* in other areas the bronchi from which they have been expelled may be recognised The bronchial mucous membrane is at times acutely inflamed, red in colour with the lining epithelial cells desquamating or it may appear pale and unaffected There is usually a certain degree of emphysema and there may be collapse of lung tissue beyond the site of obstruction

Symptoms —The disease generally begins somewhat abruptly with a cough and malaise In the course of a few days the patient becomes considerably worse, dyspnœa develops and a certain degree of pyrexia but the temperature is often not more than 99° or 100 F The dyspnœa becomes more intense and is the prominent and all important symptom The face is seen to be cyanosed the alæ nasi and the accessory respiratory muscles are in violent action, sometimes with retraction of the intercostal spaces There may be diminished movement of the chest either bilateral or unilateral If there is unilateral pulmonary collapse the heart may be slightly displaced towards the same side Vocal fremitus may be normal or locally diminished The percussion note is somewhat hyper resonant over the anterior chest wall, but behind there may be some degree of dullness over one or other lobes If the bronchi are unilaterally affected there may be dullness limited to one lower lobe with diminution of air entry and no adventitious sounds Vocal resonance over the affected area is lessened There is usually some diffuse bronchitis as indicated by the presence of rhonchi or rales Marked stridor is sometimes heard with respiration A special sign the bruit de drapeau has been described when the cast lies free in the bronchial lumen It is a dry clicking sound caused by the flapping of the cast against the wall of the bronchus as the air passes over it The ordinary sputum does not show any peculiarities It may however show Curschmann s spirals Charcot Leyden crystals and eosinophil cells and it may be absent until the crisis occurs This consists in the expectoration of the cast after a violet fit of coughing The cast may be stained with blood or there is sometimes actual hæmoptysis The peculiar nature of the expectoration often escapes notice unless it is examined by floating in water when a large intact cast is revealed The dyspnœa ceases immediately after the cast has been expelled

Complications and Sequelæ —Emphysema may occur as the result of the violent coughing or the disease may become chronic recurring at intervals of varying duration The most serious complication is laryngeal obstruction caused by the cast becoming impacted between the vocal cords

Diagnosis —The stridor and respiratory obstruction are suggestive of œdema of the glottis but auscultation will show that the site of the lesion is lower down the respiratory tract Asthma and all causes of laryngeal and tracheal obstruction must be excluded The dyspnœa and the presence of signs localised to one lobe may suggest an active lobar collapse or a lobar pneumonia but the dyspnœa is more intense than is met with in either of these conditions Casts are expectorated in diphtheria pneumonia chronic disease of the heart pulmonary tuberculosis and hæmoptysis The casts of acute fibrinous bronchitis are firmer than those found in these affections and are expectorated in long pieces showing the many branches and bifurcations of the bronchial tree

Course—The disease is generally self limited terminating with the separation and expectoration of the cast The acute stage does not as a rule continue for more than 12 to 24 hours

Prognosis—The immediate outlook is fair Death may occur in the first attack or recurrences may take place which lead to an increasing degree of emphysema with its usual results The ultimate prognosis is therefore not good

Treatment—The patient should be kept in bed and treated as a case of acute bronchitis Inhalations of medicated vapours often afford relief Potassium iodide is believed to expedite the separation of the cast Bronchoscopic removal is sometimes necessary and tracheotomy instruments should be available in case of laryngeal obstruction

2 CHRONIC BRONCHITIS

Chronic bronchitis is perhaps even more difficult to classify than the acute varieties each one of which may have its counterpart in chronic form so that the same classification may be followed At the same time it must be admitted that especially in the catarrhal forms the clinical manifestations are somewhat varied

CHRONIC CATARRHAL BRONCHITIS

Ætiology—The causes are practically identical with those of the acute form of which it is in most cases a sequel

This affection may commence at any age although it is more common in middle life and with advancing years Men are more frequently affected than women It seems also to have a special incidence in some families It is more common in damp and foggy climates and is favoured by urban conditions and by dusty occupations It starts each winter with a more or less acute catarrhal attack but each year the summer intermission becomes shorter until the bronchitis persists throughout the year It tends to produce emphysema and is aggravated in turn by this condition It is especially favoured by cardiovascular lesions such as valvular defects and arterial disease also by gout chronic nephritis syphilis and alcoholism Conditions associated with chronic cough predispose to it notably emphysema asthma arrested pulmonary tuberculosis mouth breathing and cigarette smoke inhaling

The bacteria found are practically identical with those in acute bronchitis the commonest being the pneumococcus Friedlander s pneumobacillus *N catarrhalis* streptococci and staphylococci Mixtures of two or more of these may be present

Pathology—The bronchi show chronic inflammatory changes of a catarrhal nature The walls are thickened from chronic hyperæmia and also from productive changes in the connective tissues The mucous glands may be hypertrophied or atrophied and there may be widespread desquamation of the ciliated epithelial lining of the bronchi In long standing cases there is usually some peribronchitis leading to cylindrical bronchiectasis and distortion of the bronchi by fibrosis There is almost invariably a greater or less degree of emphysema which may be generalised or only marginal Post mortem the lungs are generally red and somewhat engorged but if much emphysema has resulted they may be paler than normal On squeezing the lung after section pus or muco pus exudes from the cut bronchi and there is usually some evidence of œdema at the bases

Symptoms—A patient with chronic bronchitis complains of cough expectoration and shortness of breath on exertion The cough varies greatly in its severity During the warm weather the patient may be completely free and yet suffer for years from a winter cough It may occur frequently throughout the day and in attacks at night or only in the mornings and evenings

The expectoration varies considerably in quality and quantity so much so that

the old classifications of chronic bronchitis were based on this factor Thus there may be practically no sputum or only small tenacious pellets the ' crachats perlés of Laennec on the other hand there may be a profuse expectoration resembling unboiled white of egg diluted with water Usually the sputum is mucous or muco purulent and contains greyish black particles mixed with a frothy fluid The dyspnœa is largely due to the accompanying emphysema and so indicates the degree of chron icity of the disease At first the patient may only notice that he gets out of breath on going upstairs or on mounting slopes, but later even walking on the level causes dyspnœa

Slight rises of temperature occur in the acute exacerbations of the catarrhal process Slight cyanosis is frequently observed especially after exercise when the accessory respiratory muscles are called into play Sometimes rhonchal fremitus is felt *Movement of the chest is restricted by emphysema, and the percussion note* then becomes hyper resonant On auscultation expiration is prolonged and sonorous or sibilant rhonchi are heard all over the lungs with bubbling râles if there is thin secretion in the smaller bronchi On the other hand, rhonchi may be scanty or only occasionally heard Voice conduction is unaffected The fingers may be lightly clubbed, and further evidence of venous obstruction may be apparent in the dilated venules on the cheeks or along the costal attachments of the diaphragm

Complications and Sequelæ —The following changes may occur in the lungs—peribronchial fibrosis bronchiectasis and emphysema Asthma or attacks of bronchial spasm sometimes form a complicating factor in chronic bronchitis especially in the cases of so called bronchorrhœa Emphysema may lead to pulmonary hypertension and right heart failure *Late in the disease as the result of the cyanosis* a peculiar form of confusional delirium is met with which is worse at night

Diagnosis —Chronic bronchitis must be distinguished from pulmonary tuber culosis bronchitis secondary to heart failure, and from bronchiectasis In tuber *culosis with bronchitis there is generally wasting and often flattening* of the chest wall owing to fibrosis of the lungs In all cases where the summer intermission of the symptoms fails suddenly rather than lessens gradually tuberculosis should be sus pected The diagnosis is clinched by the presence of tubercle bacilli in the sputum *In bronchitis secondary to heart failure in addition to the cardiac signs the râles* in the lungs are chiefly basal and the rhonchi are not so universally distributed In bronchiectasis the signs are usually characteristic and often limited to one lobe The radiograph will afford useful aid in diagnosis

Course —The disease once firmly established, unless relieved by suitable climatic treatment remains chronic and becomes progressively more severe as further damage is wrought in the lungs with each hibernal exacerbation As the emphysema develops a vicious circle is initiated the aerating power of the lungs diminishes and finally cardiac failure ensues

Prognosis —The immediate prognosis is good the ultimate is bad Much depends upon the patient s social condition and opportunities for treatment espec ially in respect to climate The expectation of life of a patient suffering from chronic bronchitis is considerably shortened

Treatment —Those subject to chronic bronchitis derive benefit from life in a warm equable climate In England the south western districts are best Well to do patients can sometimes prolong their useful life by wintering in warmer climates High altitudes should be avoided if emphysema is present or if there are cardiac complications Exposure to wet and chill is dangerous The question of occupation is often difficult Much time should be spent out of doors provided that the patient *is not exposed* to the inclemencies of the elements and further, the work under taken must not involve severe muscular efforts or the inhalation of dusty or irritant particles

In England it is difficult to find an outdoor occupation conforming with these

desiderata consequently light indoor work in a good atmosphere should be advised Clothing should be warm but light and afford special protection to the chest without overloading as some patients are liable to do Excesses in diet are to be avoided also alcohol and heavy smoking The general nutrition should be well maintained and many patients especially those of spare habit seem to derive great benefit from cod liver oil during the winter months

If cough is troublesome and expectoration tenacious or scanty various combinations of expectorant remedies are useful such as ammonium carbonate or chloride tinct ipecacuanhæ preparations of squills or senega with tolu liquorice or Virginian prune as flavouring agents A simple saline mixture such as R Sodii bicarb gr 10 sodii chlorid gr 3, sp chlorof min 5 aquam anethi dest ad fl oz 1 taken with an equal quantity of hot water in the morning or at night may help to clear the tubes and give the patient a spell of freedom from cough In older patients the ether and ammonia mixture may be given and in cases with bronchial spasm potassium iodide with anti spasmodics such as stramonium lobelia belladonna or grindelia may be of great value Various antiseptic drugs such as turpentine min 10 terebene min 5 to 10 creosote min 3 in capsules or perles have been recommended and the linctus thymi et diamorphin B P C min 60 Sedative lozenges such as compound liquorice heroin or codeine are often useful in checking useless cough Intercurrent attacks of acute bronchitis must be treated on the principles described under that condition and the patient kept indoors or in bed, as may be necessary When an advanced degree of emphysema coexists the treatment appropriate to that condition should be applied When failure of the right heart ensues the treatment must be modified suitably as described under emphysema Cultivation of the sputum and testing the organisms for sensitivity may indicate appropriate antibiotic treatment which can ameliorate the condition and suppress some of the infecting agents Breathing exercises often cause great improvement for both physical and psychological reasons

CHRONIC SUPPURATIVE BRONCHITIS

Synonym —Fetid Bronchitis

Ætiology —This condition is not sharply defined and is not a specific and separate nosological entity but it is a convenient group in which to include cases with fetid purulent sputum In some forms of chronic bronchitis the secretion may from time to time accumulate in the bronchi and prove offensive on expectoration In some instances this condition becomes chronic and the expectoration is fetid up to the time of death

Pathology —There is chronic inflammation of the bronchi with marked peri bronchial thickening The bronchial secretion becomes purulent and ulceration of the bronchial wall or dilatation of the lumen may occur Post mortem the lungs are soft and on section some broncho pneumonic areas with œdema of the bases may be seen Pus of an offensive nature exudes from the cut ends of the bronchi

Symptoms —These resemble those found in chronic bronchitis with in addition the unpleasant characteristics of the sputum in which Dittrich s plugs may be found These are small yellowish bodies with an intensely offensive odour composed of compact secretion

Complications and Sequelæ —Ulceration of the bronchial walls abscess or gangrene of the lung and areas of broncho pneumonia may develop As with bronchiectasis pyæmia sometimes ensues with the formation of secondary abscesses in the brain

Diagnosis —The sputum is offensive in abscess and gangrene of the lung bronchiectasis and interlobar empyema Radiographic examination of the chest is of great value in revealing these conditions and lipiodol investigation will usually serve to distinguish between them

Course —The disease is progressive but in the early stages there may be long remissions in which the sputum is not offensive although the bronchitis persists

Prognosis —As the disease becomes firmly established the patient s strength is gradually undermined from the absorption of toxins and death ensues in the course of a few years either from exhaustion toxæmia or pyæmia

Treatment —An endeavour should be made to diminish the degree of the infection and the quality of the sputum Cultivation of the sputum will show the organisms concerned and their sensitivity to various antibiotics will decide the appropriate treatment Postural drainage is usually helpful Apart from this treatment is as *for chronic bronchitis* The offensive odour can be partially altered or masked by creosote given by mouth or by inhalation

CHRONIC SECONDARY BRONCHITIS

Chronic bronchitis is a common association of chronic cardiac and renal disease Its clinical characters do not need special description It is only necessary to emphasise as in the acute forms, the *importance of recognising* that the bronchitis is not the essential condition, and that treatment must be directed especially to the primary disease

CHRONIC BRONCHITIS FROM MECHANICAL AND CHEMICAL AGENCIES

This usually proceeds to interstitial changes in the lung and these results may be studied more conveniently under the heading of the pneumoconioses

CHRONIC FIBRINOUS BRONCHITIS

Acute fibrinous bronchitis has been described above In certain cases of chronic catarrhal bronchitis a fibrinous exudate may occur from time to time with the formation of intrabronchial casts There is then cough and dyspnœa which abate with the expectoration of the cast It therefore very closely resembles acute fibrinous bronchitis and the treatment indicated is that described above

TUMOURS OF THE BRONCHI

Tumours arising in the bronchi may be (*a*) simple or (*b*) malignant

(*a*) *Simple tumours* —The following varieties occur Adenoma lipoma myxoma papilloma and chondroma Any of these may lead to bronchial obstruction and in consequence to *collapse* or *bronchiectasis* *Adenoma* is of sufficient frequency and importance to require separate description

(*b*) *Malignant tumours* —Primary carcinoma or sarcoma may originate in the bronchi Although the majority of primary malignant tumours within the lung originate in the bronchi either from the lining epithelium or from the cells of the mucous glands their pathological effects and clinical manifestations are in the main pulmonary and it is therefore more convenient to describe them as tumours in the lung (see p 1041)

ADENOMA OF BRONCHUS

Ætiology —Adenoma of the bronchus occurs about equally in the two sexes with a slight bias to the female sex and usually in adults below the age of 40

Pathology —The tumour is at first small and of polypoid form as a rule arising in a main bronchus but not infrequently in the branch to the lower lobe *It is about twice as common on the right side as on the left* The bulbous end *is generally directed towards the trachea* The surface is usually smooth and shiny but may be

nodular An erroneous diagnosis of carcinoma was not uncommon in the past owing to differences of staining of certain of the constituent cells and their irregular distribution in the connective tissues Metastases however are unknown An adenoma often projects through the bronchial wall giving it a dumb bell or cottage loaf conformation

Clinical Features —Often the earliest symptom is hæmoptysis and this may be slight or profuse since adenomata are very vascular and bleed easily In other cases the tumour causes bronchial obstruction with resultant cough and wheezing proceeding later to pulmonary collapse or bronchiectasis Dry pleurisy may be an early result of infection and at times pleural effusion or empyema may conceal the underlying cause

Diagnosis —Other causes of hæmoptysis must be considered such as pulmonary tuberculosis mitral stenosis dry bronchiectasis or bronchial carcinoma Pulmonary collapse may suggest an unresolved pneumonia In cases with pleural effusion or empyema the diagnosis is liable to be overlooked The injection of lipiodol or tomography will often reveal a blocked or deformed bronchus but the diagnosis can only be established by microscopical examination of a portion of the tumour removed through a bronchoscope

Prognosis —This varies with the stage at which the diagnosis is established If the condition is recognised early and treated before the growth has extended outwards through the bronchial wall and before bronchial obstruction and septic infection have occurred the outlook is favourable

Treatment —Lobectomy or if necessary pneumonectomy is now the treatment generally adopted especially if secondary bronchiectasis or fibrosis has developed Piecemeal removal through a bronchoscope is now seldom employed owing to the risks of hæmorrhage and of local recurrence

THE INFECTIVE GRANULOMATA

SYPHILIS —During the secondary stage a generalised hyperæmia of the bronchial mucous membrane may occur giving rise to slight bronchial catarrh with the usual symptoms and signs a condition that has been called syphilitic bronchitis It is frequently beneficially influenced by antisyphilitic treatment In the tertiary stage gummata may form in or near the large bronchi They tend rather to fibrosis and contraction than to softening and ulceration although the latter processes may occur Contraction may lead to bronchial stenosis with the symptoms and signs described below or to extensive peribronchial inflammation and bronchiectasis If the gummata extend into the lung as may happen in rare instances destructive lesions with cough expectoration and hæmorrhage may result This condition is more fully described in the section on pulmonary syphilis (see p 1040)

TUBERCULOSIS of the bronchi occurs as part of pulmonary tuberculosis and does not require separate description It may lead to bronchial stenosis pulmonary collapse and bronchiectasis

LEPROSY —The bronchi may be involved in this disease with the production of cellular infiltration and even nodule formation At first these lesions may produce bronchitis and they are progressive leading to cough expectoration wasting and asthenia The general clinical picture may simulate chronic pulmonary tuberculosis from which it is distinguished by the presence of leprous lesions elsewhere and the absence of tubercle bacilli from the sputum

BRONCHIAL STENOSIS AND OBSTRUCTION

Obstruction of the main bronchi or of their subdivisions within the lungs may arise from causes within the bronchi or from conditions outside them and these

Course—The disease is progressive but in the early stages there may be long remissions in which the sputum is not offensive although the bronchitis persists

Prognosis—As the disease becomes firmly established the patient's strength is gradually undermined from the absorption of toxins and death ensues in the course of a few years, either from exhaustion toxæmia or pyæmia

Treatment—An endeavour should be made to diminish the degree of the infection and the quality of the sputum Cultivation of the sputum will show the organisms concerned and their sensitivity to various antibiotics will decide the appropriate treatment Postural drainage is usually helpful Apart from this, treatment is as for chronic bronchitis The offensive odour can be partially altered or masked by creosote given by mouth or by inhalation

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In most cases pain discomfort and cough develop rapidly The cough may lead to the expulsion of the foreign body or may cause dyspnœa if it forces it up to the larynx The cough soon becomes noisy often paroxysmal and if local septic changes are set up expectoration occurs sometimes mucoid and copious at others muco purulent Hæmoptysis is not uncommon Pain may be absent but is often severe The temperature is generally normal for the first few hours but soon rises especially if bronchitis pneumonia or broncho pneumonia develop The further symptoms are those of the reactive changes and complications which ensue

The physical signs naturally depend upon the bronchus affected and upon the degree of obstruction They are at first those of deficient air entry The affected side may show less movement and there may be some recession of the lower inter costal spaces in young people If a large bronchus is involved and collapse results there is some displacement of the heart to the affected side Vocal fremitus may be diminished or absent the percussion note impaired and the breath sounds and voice sounds weak or absent over the whole or part of one lung almost invariably the lower lobe If the obstruction is valvular—*i e* allowing air to pass during inspiration and not during expiration—the lung behind the obstruction may become blown up and give the physical signs of localised emphysema The presence of an obstruction in a bronchus may cause a localised wheeze or rhoncus When bronchiectasis empyema or other conditions develop their characteristic signs become apparent

Complications and Sequelæ —These have been enumerated in describing the pathological results Sometimes septic meningitis or cerebral abscess develops

Diagnosis —The history of disappearance of some article from the mouth in the act of laughing breathing yawning coughing or sighing should always arouse suspicion of an inhaled foreign body If signs indicating bronchial obstruction are found the diagnosis is almost certain In every suspicious case radiographs of the chest should be taken in two different directions in case the shadow may be merged in that of the scapula or of the ribs The possibility of a foreign body should always be borne in mind in cases of unilateral basic bronchiectasis especially if no obvious cause can be found When such unilateral lung signs develop after an anæsthetic or after operations on the mouth or naso pharynx the possibility of some inhaled material should always be remembered

Course —Spontaneous relief may occur in two ways either by the foreign body being coughed up as may happen within a few hours or days or after an interval of months or years or the foreign body may track through the lungs and pleura and be discharged in an abscess bursting through the chest wall In both cases if an interval of more than days occurs irrecoverable damage may have resulted Apart from these occurrences and from successful treatment the course is very variable Death may occur quickly from some of the septic complications or after a longer or shorter interval from bronchiectasis gangrene or cerebral abscess

Prognosis —This is grave unless the foreign body is removed within 36 hours owing to the various dangerous complications that may ensue Excluding the few cases in which cure occurs by spontaneous discharge of the foreign body about 50 per cent of cases left untreated die within 1 or 2 years

Treatment —This consists in removal if practicable as soon as possible after the diagnosis is established If the foreign body is in a main bronchus or one of its principal divisions it can usually be removed by means of the bronchoscope and appropriate forceps In case of failure the question of pneumotomy may have to be considered If this is decided on every effort must be made to localise the foreign body by radiographic examination If intra pulmonary or pleural suppuration has occurred this must be dealt with surgically and sometimes the foreign body can be removed at the same time The medical treatment of the cases consists in that of the various conditions resulting

require separate consideration It is important to emphasise the fact that in both conditions the symptoms differ according to whether the obstruction is sudden and complete in which case collapse of the corresponding lung is the rule or whether it is partial and more gradual when bronchiectasis usually results Obstruction of the smaller bronchi may result from spasm as in asthma (see p 977) or from disease as in small tube and capillary bronchitis (see p 965)

(a) INTERNAL CAUSES

These are most conveniently considered in two groups—(1) Foreign bodies, (2) those due to disease or cicatrisation of the bronchial walls

(1) FOREIGN BODIES IN THE BRONCHI

These usually gain access through the larynx and trachea by inhalation Any inhaled foreign body that is small enough to pass down the trachea may reach a main bronchus, more commonly the right or if it is small it may pass into one of the secondary bronchi It may at once become impacted, or be moved by cough but unless it is expelled in this way it is sooner or later drawn into the smallest bronchus that will receive it and there becomes impacted

The recorded varieties of foreign body thus reaching the bronchi are very numerous but among the more common are pieces of bone beads pins coins ear rings studs, pencils fruit stones grains grasses beans nuts teeth and pieces of tonsil or adenoid growths after tonsillectomy Even a living fish has been inhaled into a bronchus Foreign bodies may reach the bronchi through a tracheotomy wound or a gland may ulcerate into the lumen of a bronchus Broncholiths and pneumoliths calcareous particles originating in the bronchi and lungs respectively may be inhaled *into a bronchus instead of being expectorated*

Pathology —The pathological changes resulting from a foreign body in a bronchus depend upon the nature of the foreign body the duration of its stay the size of the bronchus obstructed by it and the degree of obstruction induced If the foreign body is smooth and comparatively little septic and if it be removed within 24 hours or so complete recovery after a very mild local inflammatory reaction may be expected If on the other hand the foreign body is rough or soft and laden with septic organisms, acute pneumonic processes often septic in character may develop very rapidly A soft type of foreign body may swell and completely obstruct the bronchus it reaches leading to complete collapse of the corresponding lung area often the whole or half of the lower lobe If the stay of any foreign body is prolonged to days weeks months or longer irreparable damage almost invariably results The forms this may take are numerous Collapse and septic pneumonia have already been mentioned If the obstruction is partial septic bronchitis with stagnation of the bronchial exudate and pus behind the obstruction leads in turn to peribronchitis bronchiectasis and fibroid induration of the corresponding lung area In other cases gangrene of the lung results Not infrequently an empyema may occur and the foreign body may be found in the empyema cavity Suppuration round a foreign body may lead to localised intrapulmonary suppuration or abscess Simple bronchial obstruction uncomplicated by sepsis may lead to bronchiectasis owing to the resultant lowering of intrapleural pressure

Symptoms —During the passage of the foreign body through the larynx and trachea urgent symptoms may occur which leave no doubt as to what has happened but this is not invariable and the patient may not be sure whether he has inhaled or swallowed it In any case after a bronchus has been reached there may be a latent period which engenders a false sense of security and leads to delay in treatment

nant growth aneurysm of the aorta mediastinal abscess pericardial effusion and œsophageal new growths (2) *Intra pulmonary causes* generally primary or secondary new growths

Symptoms—These are practically identical with those just described but in addition there are those of the condition causing the pressure

Diagnosis—This has been discussed in the previous section The broncho scope should not be employed where there is any suspicion of an aneurysm

Prognosis—This is extremely unfavourable except in cases due to tuberculous glands and pericardial effusion and in some cases of mediastinal suppuration

Treatment—This can only be palliative in the majority of cases Useless cough may be checked by a sedative linctus of diamorphine (heroin) or morphine Dyspnœa when due to spasm may be lessened by inhalations of creosote and spirits of chloro form or by administration of oxygen Pain may be relieved by aspirin or other analgesic drugs Deep X ray therapy is of value in some of the malignant cases and should be tried in Hodgkin s disease or lymphosarcoma

ASTHMA

The term asthma has been loosely employed to denote any form of dyspnœa of expiratory type occurring in paroxysms For all conditions other than that now to be described some descriptive qualification should be employed to avoid confusion

Asthma or true spasmodic asthma is a paroxysmal affection occurring most frequently in patients of neuropathic inheritance It manifests itself in attacks of severe expiratory dyspnœa due to excessive vagal discharges set free by peripheral irritation chemical agencies or cerebral influences

Ætiology—Probably no other disease shows such a varied and complex causa tion but studies of idiosyncrasy and anaphylaxis have served to explain many of the obscurities

Predisposing causes—*Age*—The first attack may occur at any age even as early as the period of the first dentition The majority of cases begin before the age of 25

Sex—Asthma is generally stated to be nearly twice as frequent in the male sex as in the female

Heredity—Asthma certainly runs in families The heredity is not always direct the nervous instability sometimes being evidenced in other generations by migraine epilepsy or hysteria The view that hypersensitiveness to certain proteins is inherited is now discredited and it is believed that an unduly irritable bronchial centre is the factor transmitted by heredity

Other diseases—Bronchitis not infrequently leads to paroxysms in patients with asthmatic tendencies Tuberculosis of the lung occasionally induces it but here again it is probably in patients with the asthmatic diathesis

Climate and locality—Asthmatics seem very sensitive to both of these but no general relationship can be proved as the effects are most variable Some patients are better in dry others in damp foggy climates and in regard to locality each patient is a law to himself

Conditions of the nose and naso pharynx—Nasal obstruction from swelling of the turbinates deflection of the septum spurs and polypi and conditions of the naso pharynx such as adenoids and enlarged tonsils undoubtedly predispose to asthma and may also be exciting causes of the actual paroxysm

Exciting causes—Chemical substances—The emanations from certain animals may be the determining cause The best known of these are the horse and cat but rabbits hares guinea pigs deer dogs and monkeys may have a similar effect Even human hair appears capable of discharging the paroxysm The dust from some substances such as corn rice or oats the smell of certain drugs such as ipecacuanha,

(2) OBSTRUCTION OR STENOSIS FROM DISEASE OR CICATRISATION OF THE BRONCHIAL WALL

Ætiology —Primary bronchial new growths including adenoma columnar celled carcinoma oat celled tumour and squamous celled carcinoma lead to bronchial obstruction at an early stage These conditions produce symptoms and signs practically identical with those of new growths in the lung (see p 1041)

A plug of mucus or a blood clot may cause temporary obstruction of a large bronchus

The causes of cicatrisation are those leading to ulceration of the bronchial wall with subsequent healing such as syphilitic processes in and around the bronchi ulceration from injury produced by a foreign body or in its removal or by the inhalation of severe irritants Bronchial tuberculosis and the fibroid variety of pulmonary tuberculosis may also produce it

Pathology —The stenosis may occur in one of the main bronchi or in one passing to a lobe or to part of a lobe At first partial it may progress until the lumen is almost completely occluded at one point The changes occurring in the lung beyond the obstruction vary with its degree At first there is retention of secretion in the bronchi and air may be forced past the obstruction in inspiration but not expelled during expiration producing emphysema with gradual bronchial dilatation When the obstruction is more complete the air is absorbed the lung tissue gradually becomes fibrotic and the bronchi dilate further

Symptoms —Cough not infrequently of paroxysmal character is an early symptom and is usually a continuation of that caused by the primary condition It may be dry or associated with mucoid sputum sometimes blood streaked The expectoration may cause dyspnœa by obstructing the narrowed bronchus If bronchiectasis develops the sputum usually becomes fetid

The physical signs are those of collapse of a part of the lung and are progressive Local limitation of movement and flattening with displacement of the heart to the affected side may be apparent on inspection The vocal fremitus is diminished the percussion note impaired at first may progress to complete dullness when fibrosis develops The breath sounds are weak or even absent and the voice sounds diminished In the early stages a bronchial stridor may be audible Compensatory emphysema of the adjacent healthy lung tissue often develops

Complications —These are similar to those in stenosis from a foreign body, notably fibrosis and bronchiectasis

Diagnosis —Bronchial cicatrisation must be differentiated from obstruction due to extrabronchial causes such as pressure from new growths aneurysm and the other mediastinal conditions mentioned in the section below The history the physical signs and examination by radiography and if necessary by the bronchoscope may help in distinguishing The Wassermann reaction should be investigated in every case where the stenosis is proved to be of intrabronchial origin

Course —Unless the primary condition causing the stenosis is one which can be arrested by treatment the condition is progressive and eventually the area of lung beyond the obstruction becomes permanently functionless

Prognosis —This varies with the cause It is most favourable in cases due to syphilis submitted to treatment at an early stage

Treatment —Vigorous antisyphilitic treatment should be employed in cases due to syphilis In other cases the treatment is to relieve symptoms by appropriate measures Cases complicated by bronchiectasis are suitable for lobectomy

(b) EXTERNAL CAUSES

These may be subdivided into—(1) *Mediastinal conditions* chiefly enlargement of the bronchial or mediastinal glands from tuberculosis Hodgkin s disease or malig

include restlessness, irritability mental exaltation less frequently depression itching of the nose or chin flatulence or polyuria Some attacks are ushered in by coryza Such warnings are not constant and the sufferer usually wakes from sleep with a feeling of suffocation In early attacks great restlessness anxiety and alarm occur The difficulty in breathing and the sense of suffocation increase the patient sits up in bed or gets up to throw open the window and fixes his arms to bring into action all possible muscles of respiration Respiration although laboured and difficult is often slow inspiration being short while expiration is greatly prolonged Both are accompanied by loud wheezing sounds audible at a distance from the chest The patient appears pale but the lips are dusky and the expression is anxious and distressed The jugular veins are distended and prominent The accessory muscles of respiration are seen to be in violent action notably the sterno mastoids scalenes and pectorals The skin is moist and there may be marked sweating The chest is much distended and at each violent attempt at inspiration very little further enlargement occurs while there is often sucking in of the supra clavicular and lower costal regions

Percussion reveals marked hyper resonance and encroachment on the cardiac and hepatic dullness On auscultation inspiration is short and high pitched expiration very prolonged and both are obscured by abundant sonorous and sibilant rhonchi and later by bubbling râles at the bases The pulse is small quick and sometimes irregular There is usually marked epigastric pulsation A differential blood count during an attack may show an eosinophilia of as much as 35 per cent Cough does not develop until late in the paroxysm and is quickly followed in many cases by the expectoration of small pellets called perles by Laennec and often likened to boiled sago or tapioca These were carefully studied by Curschmann and when examined on glass on a black background prove to consist of a central highly refractive mucinoid coil with masses and threads of mucin wrapped spirally around it Microscopically leucocytes mostly eosinophils may be seen entangled in the mucus The sputum frequently contains Charcot Leyden crystals which are now accepted as spermin phosphate With the onset of expectoration the dyspnœa quickly lessens and the attack subsides The patient often passes a large quantity of pale urine and then may sleep until morning awaking in apparent comfort More frequently he appears pale tired and anxious

Diagnosis —*This involves the differentiation from other forms of dyspnœa* particularly those of spasmodic expiratory type The chief forms of paroxysmal expiratory dyspnœa are

1 *Bronchial asthma or spasmodic dyspnœa complicating chronic bronchitis and emphysema* —This condition is sometimes a late result of true asthma but may occur independently The dyspnœa is more persistent and is more definitely related to the bronchitic attacks being therefore more common in the winter

2 *Cardiac dyspnœa or cardiac asthma* —This like true asthma is usually nocturnal but the signs of failure of compensation in association with valvular or myocardial disease usually make the nature of the dyspnœa clear

3 *Uræmic dyspnœa or renal asthma* —This is also not infrequently nocturnal and may be almost indistinguishable from true asthma Examination of the urine the urea and non protein nitrogen content of the blood usually enable the distinction to be made with certainty Cardio vascular changes with high blood pressure are frequently but not invariably present

4 *Hay asthma* is probably only a severe form of hay fever and is to be regarded as a variety of true asthma

5 *Pulmonary tuberculosis may be associated with asthmatic dyspnœa* —The differentiation may not be easy during the attack but the persistence of apical signs in the interval may give a clue It is a wise precaution *to X ray the chest of all patients* with asthma when first seen and at intervals if there are suspicious symptoms

The dyspnœa of laryngeal or tracheal obstruction and of mediastinal pressure can

and the scent and the pollen of grasses and flowers may act in a similar fashion as also may articles of diet and many drugs It is claimed that at least 50 per cent of asthmatics show hypersensitiveness to various protein antigens obtainable from animals, grains, bacterial bodies foods and drugs and over a hundred are now available for routine testing of these patients The analogy with the causation of hay fever and paroxysmal sneezing is obvious This group has been referred to as "allergic asthma

Peripheral irritation —As already mentioned irritation of the nose naso pharynx and bronchi may be asthmogenic in those of asthmatic tendency

Gastro intestinal disturbance —This is well recognised as a cause and most asthmatics find by experience the penalties of a heavy late meal and of indigestible articles of diet It is possible that actual metabolic errors may be a factor as in the so called 'week end asthma', due to altered conditions of diet and exercise at this period

Ovarian disturbance —Asthma may occur fairly regularly about 10 days before the onset of each period This is probably due to lack of progesterone from a primary ovarian defect or from an insufficient production of the gonado tropic luteinising hormone produced in the pituitary Satisfactory results are usually obtained by the injection of a preparation such as Synergon 1 ml containing 10 mg of progesterone and 1 mg of œstrone per ml This may be injected every other day during the 8 days before the period is due

Cutaneous —Asthmatics are peculiarly liable to urticaria and eczema, although these conditions usually alternate with the asthmatic attacks

Nervous factors —Fatigue emotion and nervous shock may precipitate an attack This factor cannot be ignored even in cases due to protein hypersensitiveness as is shown by a well known case in which a patient susceptible to roses developed asthma when handed an artificial rose

Pathology —Numerous theories have been propounded to explain the asthmatic paroxysm Among these may be mentioned vascular turgescence of the bronchial mucous membrane spasm of the bronchial muscle and increased secretion of the mucous glands Spasm of the diaphragm or of the inspiratory muscles has also been suggested That bronchial spasm plays the major part seems to have been established by the experiments of Brodie and Dixon and this view is strongly supported by their observations on the effects of drugs on the bronchial musculature Muscarine pilocarpine and physostigmine produce bronchial constriction and asthmatic symptoms in animals while atropine hyoscyamine and chloroform abolish these effects

There can now be little doubt that the broncho constrictor fibres of the vagus are the channel by which the impulses discharging the asthmatic paroxysm reach the bronchi although the possibility that impulses leading to vaso dilatation and to increased bronchial secretion are also concerned must be admitted

Anaphylaxis —The important part played by extraneous proteins in the genesis of asthma and the obvious analogy between the asthmatic paroxysm and the symptoms of anaphylactic shock have suggested that in many cases if not in all asthma is an anaphylactic phenomenon Evidence is accumulating in support of this view It has been shown that the lungs of the guinea pig killed in anaphylactic shock show extreme constriction of the bronchioles Asthmatics are well known to show anaphylactic tendencies and especial care in the administration of antitoxic serums is necessary with them It is of some interest to note that the Eppinger and Hess group of vagotonics show urticaria dermatographia eosinophilia and liability to anaphylactic shock all conditions which occur in asthmatics It is tempting therefore to assume that the foreign protein or toxin produces the asthmatic attack by inducing vagotonicity Further research is needed before it can be accepted that anaphylaxis accounts for all cases of asthma but it is almost certainly an important factor in many

Symptoms —The asthmatic paroxysm most commonly commences about 2 a m or later but it may sometimes develop in the daytime There are often preliminary indications some hours beforehand constituting the asthmatic aura These

Cortisone and corticotrophin are sometimes said to be most efficacious The value of these substances in this condition is not fully established but they should be tried if relief is not given by other remedies The recommended dose of cortisone by mouth is 300 mg on the first day, 200 mg on the second day, 100 mg on the third day and thereafter 75 mg daily

Many expectorant and anti spasmodic drugs have been used in treatment, potassium iodide and bicarbonate with tincture of stramonium hyoscyamus or lobelia is sometimes found comforting Suitable sedatives are paraldehyde phenobarbitone or sodium amytal in moderate doses Morphine should never be given to an asthmatic at any stage In an early stage it will cause addiction in an advanced stage it may and often does cause death

(*b*) *Between the attacks*—General advice—Asthmatics should be taught to live as normal a life as is possible under the circumstances There is usually no reason to restrict either their activities or diet although patients who have nocturnal attacks find that heavy meals at night precipitate attacks and they may therefore find it advisable to have their main meal in the middle of the day Attempts to find health by changing houses and occupation are not usually successful in themselves Migrants *from the towns in search of health are crossed by migrants from the country* with similar intentions and the benefits derived from the change seem to be equally divided between the two groups

It has been observed that some patients are sensitive to contact with certain allergens mostly of a protein nature such as pollen animal and vegetable hair house dusts and similar substances From this observation has risen the suggestion that nearly all cases are attributable to one or more sensitisations of this nature that these sensitisations can often be detected by performing skin tests with a wide range of protein substances and that desensitisation can be carried out by injecting small doses of the sensitising agents and by increasing the dose until desensitisation is achieved The theory of this treatment is an attractive one and a vast literature has grown up on the subject

Similar importance has been given to treatment with autogenous vaccines prepared from the sputum or with stock vaccines It is doubtful whether either of these two methods of treatment have anything more than a psychological value and while apparent improvement frequently takes place during such treatment it is more often due to the psychological effect of an impressive treatment and the personality of the doctor than to any desensitising effect

Attempts are made to treat patients by special diets Children are the especial victims of this form of therapy There is little evidence that bronchial asthma is ever caused by the ingestion of any particular food substance although such ingestion occasionally causes alimentary symptoms The effect of these diets is often to make patients even more introspective than they naturally tend to be

Exaggerated attempts are sometimes made to render allergen free the atmosphere in which the patient lives or sleeps Such measures condemn the patient to discomfort and disappointment The fact that many sufferers from asthma also suffer from rhinorrhœa have nasal polyps deflected septa or sinus infection has led to many misguided surgical and electrical misadventures All these treatments and many others had and have their strong adherents amongst doctors and even patients

There is an especial difficulty in assessing the value of any special treatment in asthma since the natural history of the disease is so variable and sufferers from it are so susceptible to suggestion In default of any specific treatment there are general measures and advice which are helpful The patient should be advised to try and not let his asthma dominate his life Children should go to normal schools and play games as normally as possible There is no need for a special diet except that patients are usually well advised not to have a heavy meal in the evening as a full stomach when recumbent appears to cause attacks They should avoid dusty house cleaning

usually be recognised by the fact that it is chiefly of inspiratory type and may be associated with stridor instead of wheezing In all cases of doubt the chest should be examined radiographically to exclude aneurysm retrosternal goitre or new growth

Course, Complications and Sequelæ—Such an attack may last from a few minutes to several hours and may remit and then return When the spasm is very severe and prolonged into hours with little or no remission, the condition is often termed status asthmaticus The patient may be extremely ill and death may occur unless the attack remits spontaneously or as a result of treatment More often the attacks recur at the same time each night for a considerable period extending to weeks, and then pass off, after which the patient may enjoy a period of freedom of weeks or months The intermissions may become shorter with successive attacks and increasing emphysema may develop This in turn leads to secondary bronchitis which persists together with some degree of permanent œdema of the bases Later still the cardio vascular changes incidental to emphysema occur as sequels, namely engorgement of the right heart tricuspid regurgitation venous stasis ascites and œdema Chronic asthmatics frequently present a characteristic appearance Of thin build, with sallow complexion anxious expression and nervous manner, they often have a long neck, high straight shoulders and a forward stoop Asthma necessarily imposes limitations upon those who suffer from it at all severely although many asthmatics lead active useful lives in spite of their disease

Prognosis —*When the disease starts in childhood or in early adult life it may* stop spontaneously or be relieved permanently when some causal condition is dis covered and treated During a severe attack the aspect of the patient may be so alarming that a fatal issue may seem imminent yet death rarely occurs In chronic cases the ultimate prognosis is made more serious by the complicating emphysema and bronchitis and in spite of popular belief the asthmatic has less than the normal expectation of life

Treatment—(*a*) *During the attack*—The list of anti spasmodic drugs and meas ures employed is a long one and it is impossible to foretell which will be efficacious for asthmatics vary as widely in their response to drugs as they do in regard to asthmo genic causes Drugs may be administered for this purpose by inhalation by nasal sprays by the mouth or by hypodermic injection Adrenaline hydrochloride in doses of 2 to 5 minims of a 1 in 1000 solution hypodermically may act with dramatic efficacy if administered sufficiently early, but it should be given cautiously to elderly asthmatics It may also be combined with pituitary extract as in the special prepara tions Evatmine Pitrenalin and Kadamysin In status asthmaticus the procedure suggested by Hurst may give relief A syringe of 1 ml capacity is filled with adrenaline solution 1 in 1000 This is slowly injected over a period of several minutes to half an hour or until the spasm relaxes When relief has been obtained a preparation with a more prolonged action may be used such as adrenaline mucate (hyperduric adrenalin) or adrenaline combined with chlorbutol and glycerin (adrenutol) An intramuscular injection of 0 5–1 0 ml of one of these will help to prevent a recurrence for 6–8 hours Ephedrine hydrochloride in tablets of gr $\frac{1}{2}$ to $\frac{3}{4}$ has proved itself a useful substitute for adrenaline in some cases and can be given by the mouth Pseudo ephedrine in doses of gr $\frac{1}{2}$ to 1 is often helpful where ephedrine fails Adrenaline often proves helpful as a nasal spray especially in combination with Chloretone Intravenous injections of 50 or 100 mg of nicotinic acid may give relief when adrenaline fails An oxygen tent is sometimes of great value in the treatment of status asthmaticus Intravenous aminophylline in doses of 0 25 g in 10 ml of distilled water is often effec tive especially when intramuscular adrenaline has failed It may also be given in doses of 0 5 g per rectum

It is often advisable to move cases in status asthmaticus to hospital or nursing home The change of surroundings and the different psychological atmosphere often relieves the condition

considered (1) The most important is the localised collapse which leads to secondary bronchial dilatation (2) Weakening of the bronchial walls Most of the conditions preceding bronchiectasis tend to induce severe bronchitis and peribronchitis and thus render the walls more yielding Where stagnation of secretion occurs septic and putrefactive organisms develop producing tryptic ferments which may act injuriously upon the lining membrane (3) Increased pressure on the walls thus weakened is the determining factor This is generally expiratory in origin and due to the strain of cough The actual pressure of secretion accumulating behind an obstruction may promote yielding of the bronchial walls In cases of bronchiectasis following on collapse of the lung the force of inspiration has been regarded as contributory but this is doubtful and in any case is less important than the expiratory strain of cough (4) The fourth possibility is the traction exerted upon the walls of the bronchi by contracting connective tissue in the surrounding fibroid lung This obviously postulates the existence of pleural adhesion which is not invariably present While this must be admitted as a possible contributory factor its importance is certainly less than that of the preceding ones

Congenital bronchiectasis is a pathological rarity and may be confused with congenital cystic disease of the lung (see p 1044) It is usually unilateral and the bronchi involved are of small size although in some cases the lung may show a large central cavity with smaller spaces around it Bronchiolectasis is also more of pathological than of clinical interest It occurs chiefly in children as the result of acute broncho pneumonic processes It is said sometimes to follow influenza and possibly tuberculosis The lung has a peculiar spongy appearance to which the name honey comb has been applied

Bronchiectasis of the larger tubes may be either cylindrical or saccular In the former condition several of the bronchi are more or les uniformly dilated and when opened out they appear like the fingers of a glove Sometimes the dilatations are fusiform at others they show a beaded arrangement described as moniliform These forms of dilatation are usually associated with emphysema and chronic bronchitis Saccular bronchiectasis is generally localised and may be found in any part of the lung but is most common in the lower lobes and near the base This is partly due to the fact that the antecedent processes fall with special stress on the bases of the lung and partly to the influence of gravity in leading to retention of secretions in these parts Although it may be unilateral in origin it often spreads and may involve both bases or even all the lobes There may be one large irregular cavity or a series of smaller globular dilatations involving the whole or part of the walls of one or more bronchi The cavities are usually filled with the fetid secretion to be described under expectoration When this is washed away the walls are found to be thin smooth and formed of thinned out mucous membrane In places this may have ulcerated owing to the tryptic action of the secretion and the lung tissue is thus exposed An abscess may then form and an aneurysm sometimes develops as in a tuberculous cavity The openings of the smaller bronchi derived from the dilated bronchus can often be recognised in its walls In doubtful cases the histological demonstration of cartilage and muscle in the walls establishes the bronchial origin of a cavity The surrounding lung tissue is usually airless and fibroid and sometimes is almost of leathery consistence Occasionally however it is emphysematous congested or pneumonic In the great majority of cases there is a dense pleural adhesion over the area of lung involved

Other morbid conditions found post mortem include lardaceous disease gangrene of the lung empyema pyo pneumothorax suppurative pericarditis and cerebral or spinal cord abscess Owing to the obstruction of the pulmonary circulation which may result engorgement and dilatation of the right side of the heart, tricuspid regurgitation and the results of systemic venous stasis are often found

Symptoms —The onset is usually insidious the symptoms developing during

and keep out of dusty atmospheres If they are sensitive to horse dandruff vegetable pollens or other single substances they should avoid them and the patients usually recognise these substances without having to have skin tests to identify them They should receive instruction in the use of ephedrine or if this is ineffective or loses its effect adrenaline by injection or by inhalation Knowledge that one has the means of relief at the outset of an attack often means that the attack will not develop Many of the proprietary inhalants and patent inhalers are quite effective if used early enough Most patients benefit from instruction in expiratory breathing exercises which may of course act by suggestion but which also have a manifest effect on the mobility of the chest and the respiratory excursion

Advice to change a patient s home or occupation should not be given lightly Such steps are rarely effective unless there is some very real and obvious domestic or occupational hazard

Cortisone and corticotrophin are not usually required in the treatment of chronic asthma but they have been used with great benefit at times when all other measures have failed Cortisone may be administered orally in such cases in the form of cortisone acetate tablets An initial dose of 200 mg followed by 100 mg daily for 2 or 3 days may be necessary at the commencement of treatment Thereafter symptoms can usually be controlled by quite small doses 25 mg to 50 mg at bedtime usually being sufficient

BRONCHIECTASIS

Definition —Bronchiectasis is a condition of permanent dilatation of one or more bronchi When it occurs in the finer divisions it is sometimes described as bronchiolectasis

Ætiology —Bronchiectasis is invariably secondary and may result from disease of the bronchi, the lung parenchyma or the pleura Even the rare congenital cases are probably consequent on malformation atelectasis or intra uterine disease

1 The bronchial conditions which may progress to dilatation are bronchitis, and any affection leading to partial bronchial obstruction such as plugs of mucus an inhaled foreign body a tumour (simple or malignant) stenosis from cicatrisation and external pressure from new growth or aneurysm, or enlarged bronchial glands from any cause but more especially from tuberculosis Localised pulmonary collapse thus induced seems to be the commonest antecedent condition In children measles and whooping cough are not uncommon causes especially when they follow one another in rapid succession although either alone if severe, may lead to it

2 Conditions of the lung parenchyma which may cause bronchiectasis are un resolved pneumonia broncho pneumonia collapse syphilis and tuberculosis Syphilis is rare and usually acts by leading to bronchial obstruction or stenosis Fibroid tuberculosis is a common cause but the clinical manifestations are as a rule masked by the primary condition The pulmonary complications of influenza are not in frequently followed by bronchiectasis A diffuse type of bronchiectasis is sometimes found in long standing cases of asthma

3 The pleural conditions which are followed by bronchiectasis are those which lead to pleural adhesion and those which are associated with pulmonary fibrosis notably chronic pleural thickening or empyema leading to prolonged or permanent collapse of the lung

In a lesion with such diverse antecedents the age relations are necessarily indefinite It may occur at any age but is commonest in the third and fourth decades It fre quently commences in childhood although the characteristic clinical manifestations may not develop until adult life

Sex —In most recorded statistics there is a striking preponderance in the male

Pathology —Four factors in the pathogenesis of bronchial dilatation have to be

pericarditis may develop and prove fatal Septicæmia and pyæmia sometimes occur as terminal results Cerebral abscess constitutes a serious and somewhat common complication in heavily infected cases and may be found in the frontal parietal or temporal regions or suppuration may occur in the cerebellum or cord Occasionally multiple abscesses form Lardaceous disease sometimes develops especially in the liver kidneys and intestines Multiple infective arthritis is an occasional complication

Diagnosis—In well developed basic cases this is as a rule easy The history of cough influenced by posture and associated with copious sputum is suggestive especially when variable physical signs are observed The development of the characteristic sputum with these signs renders the diagnosis almost certain and the radiograph usually serves to confirm Radiological investigation after an intra tracheal injection of 10 to 20 ml of lipiodol through the crico thyroid membrane or between two rings of the trachea under local anæsthesia or with care directly between the vocal cords has greatly facilitated the diagnosis of bronchiectasis Franklin has recommended the nasal route for the introduction of the lipiodol One nostril the oro pharynx and the larynx are anæsthetised then a gum elastic catheter is passed along the floor of the nose into the larynx Procaine or other local anæsthetic is injected down the catheter and the lipiodol follows Tilting and turning the patient in appropriate directions is done in order that the lipiodol should pass into the diseased portions of the bronchial tree The injection should be carried out in the radiographic room and the patient instructed to restrain cough if possible until the films have been taken The pictures obtained are strikingly characteristic and of great value In cases with less characteristic symptoms and signs the distinction has to be made from chronic bronchitis especially the fetid variety pulmonary tuberculosis gangrene or abscess of the lung and fetid empyema The distinction from chronic bronchitis may be difficult especially in the early stages when the sputum is not fetid but the paroxysmal cough the copious expectoration with signs including bronchial breathing and sticky râles at the base may be strongly suggestive In fetid bronchitis the fetid sputum is not constant and the cough and sputum may occur only during exacerbations of the bronchitis Pulmonary tuberculosis may give rise to difficulty particularly in cases of apical bronchiectasis Repeated examinations for tubercle bacilli and also for elastic tissue in the sputum should be made The history the mode of spread and radiographic examination may all assist It should be remembered that the two conditions may coexist and this may be suspected in some cases of fibroid tuberculosis with basic excavation Abscess and gangrene of the lung have a more acute onset and course but the chronic cavities left by these conditions may give rise to difficulty In such cases the history may be an important aid in diagnosis In fetid empyema rupturing through the lung particularly when of interlobar origin the patient is generally acutely ill there may be a history of pleurisy at the onset and possibly some evidence of mediastinal pressure or cardiac displacement The rare condition of congenital cystic disease of the lung may give rise to some difficulty (see p 1044)

Course—This depends on the extent of the bronchial involvement and the degree of infection Probably only a small percentage of cases of bronchiectasis are clinically diagnosed Those that are are usually both extensive and heavily infected Without treatment the condition tends to be progressive and leads to complications many of which are lethal

Prognosis—Surgeons and physicians tend to have different ideas about the prognosis of bronchiectasis the former are often of the opinion that without surgical treatment the prognosis is hopeless and the expectation of life short The latter are not quite so pessimistic The reason for this difference of opinion is that the surgeon tends to see a rather special selection of the worst cases the physicians see these and also many cases which are little or at all progressive

the course or as a sequel of one of the acute or chronic affections mentioned above In some few cases however they develop rapidly in patients previously in good health This is particularly the case where bronchiectasis results from an inhaled foreign body or after general anæsthesia and a rapid onset should lead to the suspicion of this The cough in well developed cases is somewhat characteristic and occurs in paroxysms These are frequently induced by change of posture—for example bending forward or lying down They occur with *special frequency on rising* and are usually associated with the expectoration of large quantities of sputum due to the *overflow of the secretion accumulated in the cavities during the night*, into a sensitive or relatively healthy bronchus, which excites cough reflexly They also occur on retiring to bed and at long intervals during the day The sputum frequently amounts to as much as 20 or 30 oz in the 24 hours It is generally extremely fetid although in the earlier stages this is not invariable The patient s breath is often also malodorous and the stench may pervade the room or even the house in which he lives although it is not persistent The patient is himself much distressed by the unpleasant character of the sputum of which he is as a rule, acutely conscious On standing in a glass vessel it can be seen to settle into three layers—a surface scum of light frothy mucus an intermediate stratum of thin turbid greenish fluid and a deep layer of brownish colour consisting of muco pus bacteria anaerobes spirochætes and *putrefactive products including foul smelling organic acids Fetid yellow bodies* called Dittrich s plugs can usually be found in the deep layer Elastic tissue is only present when erosion of the wall has occurred Hæmoptysis is not infrequent and may occasionally be fatal It may be the first and only symptom in some cases which are referred to as dry or silent bronchiectasis ✓ Dyspnœa is not as a rule apparent unless the condition is widespread or unless the pulmonary or cardiac complications are present The general condition of the patient is at first but little affected and there may be no fever for long periods As the disease progresses lassitude anorexia and some wasting slowly develop while bouts of fever occur due to retained secretions or to some complication

Physical signs vary with the extent and degree of dilatation and also with the *amount of secretion present In the early stages there is at most slight dullness at* one base with diminished air entry peculiar sticky leathery rales and diminished *vocal resonance When bronchiectasis is well developed the signs are* almost characteristic The patient may appear well nourished and of good colour although on cold days *especially in children duskiness or cyanosis is often noticeable* There is well marked clubbing of the fingers generally of drum stick character and pulmonary osteo arthropathy involving many joints sometimes *develops There may* be localised *flattening or retraction* of the chest wall over the affected area with diminished movement and the heart is drawn over to this side The *remaining signs* vary with the state of the cavity If this is full there is diminished vocal fremitus dullness and weak or absent breath sounds and voice sounds If the cavity is *empty* or partly empty the vocal fremitus is increased the percussion note is boxy or dull while the breath sounds are bronchial or cavernous Adventitious sounds are *then* generally audible the most characteristic being sharp metallic or leathery râles Bronchophony and pectoriloquy are marked and occasionally the veiled puff of Skoda can be heard Signs of bronchitis are often apparent in the adjacent lung tissues compensatory emphysema may be demonstrable in the unaffected parts of the lung *and on the opposite side* Radiographic examination before and after the injection of lipiodol serves to define the extent of the disease and the degree of fibrosis Tomography *may also be useful*

Complications and Sequelæ—The chief pulmonary complications are septic *broncho pneumonia gangrene and abscess* The pleura may become involved giving rise to dry pleurisy which sometimes progresses to empyema and rarely to pyo pneumothorax *while in other cases pleural* adhesion and contraction result Septic

DISEASES OF THE LUNGS

HYPERÆMIA AND ŒDEMA

Hyperæmia of the lungs may be either active or passive In the former there is an increased supply of arterial blood through the pulmonary and bronchial arterioles In passive hyperæmia there is engorgement of the pulmonary venous radicles and capillaries With both forms there is frequently œdema due to the exudation of serous fluid into the lung alveoli The term congestion' is sometimes employed as an alternative to hyperæmia but owing to its erroneous popular use it is best avoided

(a) ACTIVE HYPERÆMIA

Ætiology—This may occur in association with any acute inflammatory process affecting the bronchi lungs or pleura It sometimes results from the inhalation of pulmonary or bronchial irritants such as poisonous gases or heated air Severe muscular exertion and exposure to extreme cold are described as causes but the former at least is doubtful An important variety is that known as *collateral or flux ionary hyperæmia* which occurs when there is obstruction to the circulation in the whole or part of one lung from conditions such as a large or rapidly developing pleural effusion an extensive and spreading pneumonia or in association with pneumo thorax This may develop in the sound lung or in the unaffected parts of that diseased A primary form of acute hyperæmia the maladie de Woillez has been recognised by French authors but this is generally regarded as a mild or abortive pneumonia

The clinical manifestations of acute hyperæmia are merged in those of the pro cesses with which it is associated and therefore do not need separate description

(b) PASSIVE HYPERÆMIA

Ætiology—Passive hyperæmia may be produced by conditions impeding the venous return from the lungs The commonest causes of impeded return are left sided heart lesions causing overfilling of and increased pressure in the left auricle In mitral stenosis it may occur early and sometimes almost acutely but aortic and myocardial lesions also lead to it when the left ventricle fails and the mitral valve yields Direct obstruction of the pulmonary veins sometimes results from external pressure by aneurysm mediastinal tumour or enlarged bronchial glands or from obstruction of the lumen by thrombosis

Passive hyperæmia is obviously in the main dependent on mechanical factors it is not surprising therefore that gravity seems to play a part in the localisation of its effects which are usually most marked in the bases or most dependent parts of the lungs In bedridden enfeebled or old patients particularly if myocardial weak ness or degeneration coexists this factor becomes of great importance Not in frequently some degree of œdema of the bases develops and the condition is then called hypostatic congestion If such an area becomes infected the resulting process is known as hypostatic [illegible] al hyperæmia and œdema of the hypostatic type also result [illegible] ses such as enteric fever from poisoning by [illegible] al event in many cerebral lesions causing

[illegible] pillaries are engorged with the result [illegible] le the alveolar walls and septa are [illegible] ent derived from the hæmo [illegible] ited in the epithelium of the

Given morbid anatomical bronchiectasis the prognosis is uncertain but severely infected cases with much foul sputum repeated hæmoptyses and pyrexial episodes are progressive with a short expectation of life failing adequate treatment, but there are exceptions even to this

Treatment —The medical treatment of bronchiectasis consists of efforts to secure efficient emptying and drainage of the affected part of the lung to lessen or control the infective processes occurring in the lung and to promote the general health and well being of the patient Bronchograms of the affected lobe or lobes indicate the desirable position for evacuation of the lung In bronchiectasis of the lower lobes the patient either bends over or his feet are raised so that the bifurcation of the trachea is below the level of the affected lung If the anterior bronchi are affected he lies on his back and if the posterior bronchi are affected he lies on his face He should also be tilted on his side so that the affected side is uppermost The best position for drainage can usually be found by a process of trial and error The longer the appropriate position is maintained the more effective the result In any case it should be maintained for not less than 30 minutes at a time The initial instruction is best given by a qualified masseuse and the treatment must be maintained for life if the lobe is not going to be removed surgically The Nelson bed hinged in the middle is helpful in maintaining the correct posture long enough for drainage to occur

The sputum should be cultivated and the organisms identified and their drug sensitivity tested The quantity and degree of infection can be altered by the appropriate use of antibiotic preparations although the development of drug resistance reduces their effectiveness They are especially valuable during pyrexial periods of exacerbation of infection due to defective drainage Penicillin inhalations have some limited effect but no drug is really effective if the drainage from the affected bronchi is poor

Creosote given by inhalation or in capsule of 3 minims was much used in the past and it has value in helping to disguise the fœtor of the breath which is one of the most distressing features of these cases Bronchoscopic aspirations have been found effective in some cases especially those where bronchostenosis or bronchial œdema prevents effective drainage

The possibility of treatment by surgical segmental resection by lobectomy or pneumonectomy should be considered Surgeons have no doubt about the value of prophylactic surgery and may advise resection for anatomical bronchiectasis without symptoms Many physicians are not so convinced of the necessity of these resections Differences of opinion represent a different idea of the prognosis There is unanimity about the desirability of resection for the infected cases with much sputum daily with repeated pulmonary hæmorrhages or with a history of recurrent attacks of pneumonia or pyrexial episodes Thoracic surgery has had no more dramatic successes than in these cases Unfortunately in many of the worst cases the disease is too extensive for removal to be possible In these cases medical treatment palliates and prolongs life

INJURY

External trauma applied to the chest wall may cause rupture of a main bronchus This is especially liable to occur after severe crushing accidents One or other of the main bronchi may be completely severed from the trachea The chief clinical feature presented in such a case is emphysema of the neck and upper portion of the chest wall Death usually ensues in 2 to 3 days

R A YOUNG
G L BEAUMONT
F R BOLAND

of greyish yellow or pinkish fluid Frothy fluid of similar character is found in the bronchi and even in the trachea and naso pharynx in hyperacute cases

Symptoms—The onset is sudden and generally occurs when the patient is lying down hence being most frequently observed at night The patient awakes with intense dyspnœa and a sense of suffocation then frequently rolls or rushes about in the endeavour to breathe even clutching at the throat Cyanosis is present and the aspect is one of anxiety and alarm Frothy fluid often pink in colour may soon stream from mouth and nose or be brought up in great gulps The chest movements are hurried and the accessory respiratory muscles are in violent action Vocal fremitus is diminished over the lower lobes The percussion note soon becomes impaired over the lungs commencing at the bases The breath sounds are at first vesicular or harsh with prolonged expiration then become faint and may be obscured by bubbling râles or crepitations audible all over the chest Voice conduction is diminished

Complications and Sequelæ—Owing to its acute and rapid course complications do not occur Bronchitis may result as a sequela

Diagnosis—The affection is usually so characteristic that the diagnosis is obvious In the more protracted cases the dyspnœa and the physical signs are not unlike those of acute suppurative bronchitis or suffocative catarrh and broncho pneumonia but in both of these there is some degree of fever and the expectoration is less copious and when it occurs is usually of purulent or muco purulent character The nocturnal onset of œdema may suggest asthma but the physical signs and the late and scanty expectoration in the latter suffice to distinguish it

Course—The malady usually lasts only minutes or hours Unless it remits or treatment affords relief the patient rapidly becomes unconscious and death follows the heart continuing to beat after respirations have ceased

Prognosis—The prognosis is always very grave but prompt treatment has saved some cases Death may occur in less than 10 minutes or be delayed for 24 or 48 hours

Treatment—The most successful treatment is the immediate subcutaneous injection of morphine gr $\frac{1}{4}$ Good results have also followed the injection of atropine sulphate gr $\frac{1}{100}$ to $\frac{1}{60}$ hypodermically Intravenous injection of aminophylline has been recommended The dose is 0 25 g in 10 ml of distilled water Oxygen inhalation by nasal catheter or the B L B mask or oxygen tent is of value in some cases others derive no benefit from it Prompt venesection has been recommended

(*d*) CHRONIC PULMONARY ŒDEMA

This is usually the sequel of chronic passive hyperæmia and the causes and symptoms are those of that condition It may also occur in chronic renal disease In marked degrees of œdema however the signs may closely simulate those of pleural effusion save for the displacement of the cardiac impulse It is important to remember that some degree of hydrothorax may occur as a complication and increase the difficulty in diagnosis

INFARCTION OF THE LUNGS

Infarction of the lungs or pulmonary apoplexy results when a branch of the pulmonary artery becomes occluded by embolism or thrombosis

Ætiology—*Embolic forms*—The obstructing plug may originate in any part of the systemic venous system in the right side of the heart or on its valves or in the pulmonary artery itself The commonest peripheral cause of embolism is detachment of a thrombus in cases of thrombo phlebitis This may occur in the veins of

alveoli and in the fibroblasts in the inter alveolar septa In long standing cases the lung is firmer than normal and brownish red in colour a condition described as *brown induration* If any degree of œdema is present serous fluid is found in the alveoli on post mortem examination and on section of the lung frothy serous fluid exudes which may contain some of the pigmented alveolar cells constituting what are called ' cardiac cells ' Although congested and œdematous lung is heavier than normal, it usually floats in water

Symptoms —In slight degrees of hyperæmia these may be absent or negligible In more advanced cases they are those resulting from the impeded circulation through the lungs and the deficient aeration which this entails Dyspnœa is the most prominent symptom and it is generally a measure of the degree of hyperæmia It is markedly increased by exertion of any kind and in extreme degrees it is distressing and eventually alarming It may be inspiratory or expiratory in type, and in the latter case it is sometimes described as cardiac asthma In severe cases there is usually orthopnœa Cough is almost invariably present, and there is usually some expectoration of frothy fluid, which may be blood stained The pigmented cells referred to above as cardiac cells may be found in it Cyanosis is common and indicates the degree of anoxæmia This may be associated with distension of the jugular veins and there is often obvious distress As in other forms of cyanosis there is usually some increase in the number of red corpuscles The vocal fremitus at the bases may be diminished the percussion note impaired the breath sounds weak and accompanied by rhonchi crepitations or bubbling râles although these signs are for the most part due to the associated œdema In addition, the signs of the primary condition in the heart will be apparent

Complications —Pulmonary œdema and infarction are the chief complications

Diagnosis —This condition has to be distinguished from (1) chronic bronchitis in which case there may be some rise of temperature and the physical signs are more variable and more disseminated, (2) infarction in which pain and hæmoptysis of sudden onset are the rule

Course —If the venous engorgement cannot be removed it tends to become progressively worse whereas when it results from temporary cardiac embarrassment recovery is usually complete as soon as the heart function is restored

Prognosis —This is so entirely dependent upon the nature and degree of the condition responsible for the engorgement that no general rule can be formulated

Treatment —The treatment is that of heart failure with digitalis salt restriction and mercurial diuretics In elderly patients or those likely to be confined to bed for long periods, attention should be directed to the decubitus This should be changed frequently and if possible the patient should be permitted to sit up or to get into a chair and encouraged to take a few deep breaths several times during the day

(c) ACUTE OR HYPERACUTE PULMONARY ŒDEMA

In this condition flooding of the alveoli with the serous exudate from the pulmonary capillaries occurs with great rapidity

Ætiology —The most important cause of pulmonary œdema is left heart failure whether from hypertension disease of the aortic or mitral valves or coronary thrombosis Pulmonary œdema may also occur in acute cor pulmonale from pulmonary infarction It may complicate exposure to lung irritant gases or disease of the nervous system such as tumour vascular accident or trauma or intravenous transfusion or disturbance of the fluid balance in treatment with deoxycortone acetate (D O C A) cortisone or stilbœstrol Sometimes paracentesis of large effusions is followed by pulmonary œdema

Pathology —The alveoli are found to be flooded with a thin serous exudate The lungs are heavier than normal sodden and on squeezing exude large quantities

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Pathology —The alveoli are found to be flooded with a thin serous exudate The lungs are heavier than normal sodden and on squeezing exude large quantities

Symptoms—If a large embolus blocks one of the main divisions of the pulmonary artery there is sudden intense dyspnœa pain in the chest distress cyanosis and rapid unconsciousness death resulting in a few minutes from asphyxia In other cases the patient gives a short cry and falls unconscious death occurring almost immediately from syncope In some cases unconsciousness develops so rapidly and the respiratory symptoms are so little apparent that a cerebral vascular lesion may be suspected On the other hand life may be maintained for several minutes or even hours the patient being unconscious or in acute distress and anxiety with urgent dyspnœa lividity and cyanosis Respiration is deep and laboured but fails to give relief to the sense of suffocation In such cases also death may result eventually from asphyxia or syncope or the patient may slowly recover In less severe forms such as occur in cardiac and in some post operative cases there is sudden pain with difficulty in breathing followed in a few hours or in a day or two by cough with hæmoptysis or by the expectoration of deeply blood stained mucus persisting for some days and slowly clearing up If the embolus is infective fever often of hectic type results sometimes delayed for a day or more

In the severe cases there is cyanosis distension of the veins of the neck acute anxiety with exophthalmos and cold clammy skin The only physical signs apparent are the deep laboured breathing the harsh breath sounds and the evidence of cardiac embarrassment with feeble failing pulse

In less severe cases the signs are also not characteristic There are evidences of cyanosis and distress of less urgent character possibly some limitation of movement on the affected side increase of vocal fremitus localised dullness with weak or absent breath sounds and sometimes a pleural rub In some cases definite bronchial or tubular breath sounds may be audible A few fine râles are sometimes present in the adjacent lung areas

Complications and Sequelæ—Localised dry pleurisy is almost invariably present With infective emboli abscess or gangrene and later empyema may result In organisation an infarct leads to a localised area of fibrosis

Diagnosis—The dramatic onset the history and the associated lesions of the veins or heart render diagnosis easy as a rule but it may be necessary to eliminate other causes of hæmoptysis notably pulmonary tuberculosis and chronic venous hyperæmia

Radiological appearance—It is possible to have an extensive infarction without any visible radiological change and in fact it is usually the smaller lesions which can be seen in the form of small peripheral areas of opacity not very clearly defined and occasionally associated with pleural effusion The diaphragm may be raised

Course—As already described death may occur from asphyxia or syncope in the course of a few minutes or hours although recovery occurs in some very severe cases In the less severe forms after the initial urgent symptoms have passed off recovery is often rapid and uneventful save for pain cough and blood stained expectoration

Prognosis—This depends largely upon the initial shock The prognosis is very grave when the patient rapidly becomes unconscious As there is less likelihood of sepsis in cases due to cardiac lesions than in those due to localised venous thrombosis the prognosis is rather better in the former but on the other hand organisation of a clot in a vein may completely remove the source of the emboli while the source often persists when they are derived from the heart

Treatment—Morphine pethidine or papaverine should be given to allay the anxiety of the patient Atropine gr $\frac{1}{100}$ or $\frac{1}{60}$ is often given but is of doubtful value Anti coagulant therapy should be given to prevent further spread and formation of clot Heparin should be given intravenously in doses of 5000 units 4 hourly for 24 hours One of the dicoumarol derivatives such as ethyl biscoumacetate (Tromexan) or phenylindanedione (Dindevan) should be started at the same time

the lower extremity, or in those of the uterus after childbirth Thrombosis with embolic detachment may also develop in prolonged or wasting diseases such as enteric fever tuberculosis and cancer in acute processes such as influenza, septicæmia and pyæmia and in localised septic lesions such as otitis Pulmonary embolism is not infrequently observed after abdominal or pelvic operations, and after the radical cure of hernia or hæmorrhoids

Intracardiac thrombi from the right auricle or ventricle becoming detached lead to embolism and this occurs especially in cases of right sided heart failure secondary to left sided valve lesions Vegetations forming on the tricuspid or pulmonary valves in septic endocarditis on detachment produce pulmonary infarction Rarer causes are fat embolism after injury to bone or to a fatty liver, the entry of pieces of new growth or hydatid daughter cysts into systemic veins and even air embolism occurring sometimes as a complication of pneumoperitoneum It may also occur during blood transfusion if the pressure in the bottle is raised unduly by a Higginson s syringe while the filter is partially blocked Air embolism has followed insufflation of the vagina with silver picrate powder in the treatment of vaginitis and trichomonas infections

Thrombotic forms —Thrombosis occurs as a secondary process around pulmonary emboli but it is probable that some cases of infarction are due to a primary thrombosis This condition may be produced by some acute or chronic pulmonary disease, such as gangrene tuberculosis and fibrosis and by atheroma of the pulmonary artery Any process leading to chronic venous hyperæmia may also cause it A rare cause is thrombo phlebitis migrans

Pathology —Although the pulmonary arteries are not strictly speaking end arteries since there is some degree of anastomosis between them and the bronchial arterioles yet the result of their obstruction is to produce infarcts comparable with those in other organs The origin of the blood in the obstructed area has been much discussed Cohnheim regarded it as the result of regurgitation from the veins a view subsequently disproved since the infarct is hæmorrhagic even when the veins are also obstructed It is now regarded as due to influx from the anastomosing bronchial capillaries into the pulmonary capillaries and the escape of this blood from the latter owing to their altered nutrition It is generally accepted that embolism is much more common than thrombosis If a large embolus has caused sudden death it will be found arrested at the bifurcation of a large branch of the pulmonary artery or even in one of the main divisions of that vessel In such cases there has not been time for pulmonary changes to occur and the chief post mortem condition found is engorgement of the right side of the heart

In post mortem examination of cases where smaller emboli have led to infarction the infarcts are usually found in the lower lobes more commonly in the right lung They extend to the surface in the majority of cases and can be seen before section as slightly raised dark red areas with the overlying pleura a little roughened from inflammatory exudate They feel hard and firm and on section are typically wedge shaped with the base on the surface and the apex centrally placed In the rare deep seated infarcts a spheroidal form is the rule When recent an infarct is dark red in colour and suggests hæmorrhage with clot formation hence the term pulmonary apoplexy In some cases infarcts have a purplish hue and are said to resemble the colour of damson cheese later they change to brownish red Infarcted areas sink in water There may be a single large infarct almost occupying one lobe sometimes only a small one or several of varying size and age scattered throughout the lungs In some cases a fortunate section may reveal the embolus with its ensheathing thrombus but sometimes a thrombus only is found Microscopically the alveoli and finer bronchioles are filled with red blood corpuscles and there is a sharp delimitation from the healthy lung If the embolus is infective suppuration occurs and abscess or empyema ensues

The general consensus of opinion now is that collapse is due to bronchial obstruction produced by plugs of mucus foreign bodies or by swelling of the mucous membrane bronchial spasm or external pressure Paralysis of the diaphragm to which Pasteur gave the premier role does not of itself produce massive collapse although immobility or elevation of the diaphragm favours the formation of obstructive plugs on the one hand and on the other may be the result of the obstruction and consequent collapse

Synonyms —Active Lobar Collapse Massive Collapse

Ætiology —The causes are many and various Foreign bodies in the bronchial tree neoplasms of the bronchus granulomata usually tuberculous stenosis of the bronchus as a result of tuberculosis syphilis or bronchiectasis form an endobronchial group Compression of a bronchus by mediastinal tumours aneurysms or pericardial effusions form another

Then there is the much larger group of post operative and post traumatic cases and those occurring in whooping cough bronchitis asthma pneumonia and bronchiectasis In all these cases the probable common factor is obstruction by retained secretions

Barium included in post operative feeds and lipiodol inserted into the mouth during dental operations has shown that pulmonary aspiration is much commoner after operations than is generally realised

Collapse due to fluid in the bronchial tubes blood lipiodol liquid paraffin and sea water are specially mentioned because they tend to be forgotten

Collapse of the lung which frequently follows the division of adhesions in artificial pneumothorax is probably due to the trapping of retained secretion to bronchial stenosis or ulceration or a combination of these factors

Pathology —At post mortem examination the whole of the lung or a lobe or portion of a lobe may be deflated and retracted towards the hilum The collapsed area is bluish red firm does not crepitate and sinks in water There are often pneumonic and pleuritic changes but these may be either primary or secondary

In massive collapse the heart and mediastinum are displaced towards the affected side and the unaffected lobes are distended with air

Symptoms —The abruptness of onset depends on the causation and the extent of collapse Massive collapse of the whole lung and of a whole lower lobe following operation usually has a sudden onset with pain in the lower part of the thorax and behind the sternum Severe dyspnœa quickly follows and the patient appears dusky cyanosed and alarmingly ill There may be a cough but it is often unproductive The pulse and respiration rate are rapid and the temperature often rises abruptly Occasionally especially in old people the onset is more surreptitious

The physical signs of massive collapse are usually dramatic There is immobility of the affected side often with sucking in of the ribs The apex beat is displaced towards the affected side There is dullness to percussion on the affected side with hyper resonance on the unaffected The vocal fremitus is diminished or absent and the breath sounds are diminished or absent Occasionally conduction is increased with bronchial breathing and only the displacement of the apex beat and trachea gives a clue to the true diagnosis but if the obstruction is in a main bronchus these physical signs are unlikely Hilar or lobular collapse will give proportionately less physical indications

Radiological appearances —The radiological appearances are characteristic but vary with the extent and duration of the collapse There will be a homogeneous opacity varying in shape with the lobes involved accompanied by local and general compensatory emphysema deviation of the trachea and heart to the side of the lesion and elevation of the diaphragm Lateral or oblique views are essential

Complications and Sequelæ —These depend on the cause of the obstruction and vary from broncho pneumonia and pulmonary abscess to pleurisy and empyema

Tromexan 0 3 g , is given three times during the first day and after that three times a day in a dose controlled by prothrombin estimation Dindevan 0 1 g is given morning and evening for the first day and subsequently twice daily in doses controlled by daily prothrombin estimations After the prothrombin time has been brought to between 20 and 30 per cent of normal, heparin is discontinued and Tromexan or Dindevan is continued in controlled doses The danger of spontaneous *hæmorrhages* must be borne in mind *Pulmonary embolectomy has been successfully* performed, but unless the services of a surgeon with special knowledge of cardio vascular surgery are available the patient is more likely to survive if recovery is left to nature

The danger of too *great immobilisation of patients especially elderly ones,* must be borne in mind and whenever possible patients should be allowed to get out of bed for toilet purposes or allowed to sit in a suitable chair at intervals or limb exercises should be regularly performed under supervision

COLLAPSE OF THE LUNGS

In collapse of the lungs the alveoli are completely or partly devoid of air The *condition may be congenital and due to non expansion of the lung* when it is re ferred to as atelectasis On the other hand, collapse may be the result of removal of the air from lung tissue previously expanded, when it is called apneumatosis or acquired collapse The three terms—collapse atelectasis and apneumatosis—are however used as *synonyms by many writers*

ATELECTASIS OR CONGENITAL COLLAPSE

Ætiology—This condition occurs in still born and in premature infants and probably persists to some degree for weeks or even months in weakly children *It* may result from immaturity or from weakness of the inspiratory muscles and from obstruction of the air passages by mucus and meconium It may be a consequence of disease such as congenital syphilis or lesions and developmental defects of the *nervous system*

Pathology—Atelectasis is due to failure of the respiratory mechanism to draw air into the alveoli and expand them as occurs normally with the first few inspiratory efforts of the newborn infant

Atelectatic lungs are solid airless and small They are usually described as presenting appearances similar to those of adult liver as regards colour and consistence In partial atelectasis the lung appears mottled and small expanded areas of pinkish colour may project from the surface The condition is chiefly of medico legal and pathological interest

APNEUMATOSIS OR ACQUIRED COLLAPSE

There are two types of acquired collapse That due to obstruction of some part of the bronchial tree and that due to external pressure by fluid, air or diaphragmatic abnormalities These two conditions have previously been described as active and passive collapse respectively but Pasteur, who described collapse in a Bradshaw Lecture in 1908, used these terms in quite a different sense since he described as active , collapse which he thought was due to diaphragmatic paralysis and he used the term 'passive *to describe lobular collapse due to bronchial* obstruction The terms are best avoided This latter type of collapse is sometimes known as absorption collapse as opposed to relaxation or compressive collapse where the primary cause of the collapse is outside the bronchial tree

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HÆMOPTYSIS

It should be recognised that hæmoptysis is a symptom not a disease It is here considered separately because the accurate diagnosis of its origin is essential to its treatment which differs widely in different conditions

Definition—The term hæmoptysis is arbitrarily restricted to the expectoration of blood entering the air passages from structures below the larynx or from the larynx itself When the blood is derived from the naso pharynx or mouth it is sometimes described as spurious hæmoptysis

Ætiology—1 Pulmonary tuberculosis is the commonest cause, the blood being derived from an aneurysm in a pulmonary cavity or from ulceration of a small vessel or congestive processes around the early lesions

2 Chronic venous congestion particularly in mitral stenosis

3 Bronchiectasis as a result of bleeding from granulation tissue or from ulceration of the bronchiectatic walls Latent bronchiectasis without sputum may cause recurrent hæmoptysis (*forme hemoptoique sèche*) this is more common in upper lobe bronchiectasis

4 Inflammatory and destructive diseases of the lungs air passages or pleura such as pneumonia broncho pneumonia especially the influenzal variety abscess and gangrene Pneumoconiosis streptotrichosis and ulceration of the larynx trachea or bronchi from tuberculosis gumma or new growth may also be associated with hæmoptysis Breaking down of a caseous or calcareous bronchial gland is a rare cause as also is rupture of an empyema through a bronchus

5 Infarction of the lung from embolic or thrombotic obstruction

6 New growths of the lung bronchi or mediastinal glands

7 An aortic aneurysm may cause hæmoptysis by weeping through an eroded bronchus or by direct rupture the latter being of course immediately fatal

8 Traumatic causes—Injury may cause hæmoptysis by fractured ribs wounding the lung by contusion and by breaking down of healed tuberculous lesions Hæmoptysis occurs frequently in wounds of the chest both penetrating and non penetrating A foreign body such as a piece of shrapnel may lie dormant for years and then cause recurrent hæmoptysis

9 Certain abnormal blood conditions chiefly leukæmia purpura hæmophilia scurvy minor degrees of vitamin C deficiency and occasionally pernicious anæmia Hæmoptysis occasionally occurs in the malignant specific fevers especially small pox and measles

10 Parasitic causes such as pulmonary distomatosis and spirochætosis are common in Asia but rare in Europe Hydatid disease of the lung may cause repeated slight hæmorrhages

11 Vicarious menstruation—Some cases in women have been regarded as vicarious menstruation and this view dates back to Hippocrates It is probable however that most cases are to be explained as due to leakage from obscure pulmonary lesions

12 Hæmoptysis occasionally occurs in apparently healthy persons In some with high systemic arterial tension it is probable that the pulmonary arterial pressure is also raised and the condition may be regarded as analogous to the epistaxis which occurs more commonly in such patients Sometimes the hæmoptysis is due to leaking from an old arrested tuberculous lesion

13 Rupture of an hepatic abscess or hydatid cyst through the diaphragm into a bronchus is an occasional cause

14 Polyarteritis nodosa is a rare cause of pulmonary hæmorrhage

Spurious hæmoptysis is usually due to staining of the saliva or the pharyngeal secretion with blood generally derived from the gums which are spongy and congested often from early pyorrhœa The condition is common in anæmic girls and

Post operative cases which survive the abrupt onset usually make a complete recovery when the obstructing mucus is coughed up

Diagnosis —The most important conditions from which this malady has to be distinguished are lobar pneumonia pulmonary embolism pneumothorax and pleural effusion The position of the cardiac impulse is often the deciding factor in collapse it is displaced towards the lung involved, in pleural effusion and pneumothorax it moves away from the affected side whereas in lobar pneumonia there is usually no cardiac displacement, although there may be dilatation Labial herpes and blood stained expectoration are more frequently seen in pneumonia than in collapse When in right sided collapse there is marked distension of the left lung with obliteration of the normal cardiac dullness the signs superficially resemble those of a left sided *pneumothorax*, but with *careful examination no such error should be made* The distinction from pulmonary embolism may be difficult at first but the localisation of the signs and the blood stained expectoration may give useful indications

Course —The course of the affection in post operative cases or cases associated with bronchitis asthma or lobar pneumonia is rapid After periods extending from *2 to 5 days the temperature falls to normal the symptoms disappear the lung* quickly re expands the heart returns to its normal position and there is complete recovery

Treatment —Prophylactic treatment prevents the onset of post operative collapse Planned operations should not be carried out on patients with acute respiratory infections or with untreated suppurative conditions of the naso pharynx Patients should be encouraged to sit up and move as soon as possible after operation Those found to have poor pulmonary ventilation before operation should be taught breathing exercises which will be of service both before and after operation Once the collapse has occurred the object of treatment is to produce cough and expectoration and restore ventilation to the collapsed lung Tight abdominal binders or strapping should be loosened the patient laid flat on his back and gently rolled from side to side twelve times This often results in cough with expectoration of the obstructing mucus and the lung rapidly re expands This treatment (Sante manœuvre) should be repeated every 4 hours if it is not successful at the first attempt It is surprising how rapidly relief can be obtained by this simple manœuvre even in cases in which the collapse has been present for 2 or 3 days Stimulant expectorants should be given subsequently for a few days Postural drainage should be used and tapotage over the affected lung sometimes helps to dislodge the mucus and promote effective coughing Inhalation of oxygen with 7 per cent of carbon dioxide promotes deep respiration Accurate measurements of the daily sputum should be kept A diminution without clinical improvement is suggestive of recurrence of the obstruction Bronchoscopic aspiration has been recommended in cases of post operative massive collapse Usually no plugs of mucus are seen obstructing the collapsed bronchus

Collapse due to External Pressure —Pleural effusions pneumothorax and diaphragmatic displacement also produce collapse of the lung The latter operates by alveolar compression The first two operate by separating the two layers of the pleura and allowing the lung to retract This first stage is known as relaxation collapse Large effusions or pressure pneumothoraces cause compression collapse which is more complete High tension pneumothoraces in patients with a mobile mediastinum sometimes cause collapse of the peripheral portion of the contralateral lung This form of collapse is described with the conditions which cause it

COMPLETE CONGENITAL ABSENCE OF A LUNG

Complete congenital absence of a lung is a rare condition *but can be diagnosed* by radiographic examination *It is not* compatible with a normal expectation of life

While distinguishing between the various causes of hæmoptysis it is well to regard and to treat it as due to pulmonary tuberculosis until some other cause is conclusively established The sputum should be examined for tubercle bacilli on several occasions the temperature recorded and the physical signs including radio graphic appearances most carefully watched

The presence of a valvular lesion especially mitral stenosis with signs of pulmon ary engorgement may render the cause of hæmoptysis clear When tuberculosis and cardiac disease can be excluded a careful study of the history the symptoms and signs may throw light on the diagnosis or suggest some investigation which will serve to establish it *e g* examination of the sputum for parasites and hydatid hooklets the cytological examination of the blood and radiographic examination

In other cases as in bronchiectasis abscess or gangrene the history, the physical signs and the nature of the sputum are often characteristic

In the latent or silent form of bronchiectasis (*forme sèche*) the condition may be revealed only by lipiodol injection

Bronchoscopy may be of great value in revealing the presence of adenoma or carcinoma Patients who have had a hæmoptysis which has eluded diagnosis must be kept under observation with radiographic control

Prognosis —Apart from hæmoptysis due to aneurysm which is rapidly fatal or pulmonary tuberculosis the immediate prognosis in cases of pulmonary hæmor rhage is not unfavourable even when it continues for days The ultimate prognosis depends upon the cause

Treatment —This is so entirely dependent upon the cause and origin of the bleeding that reference should be made to the corresponding diseases

EMPHYSEMA OF THE LUNGS

Emphysema of the lungs or alveolar ectasis is a condition of distension of the alveoli it is usually progressive and is associated with definite changes in the inter alveolar walls The following varieties are generally recognised—(1) large lunged or hypertrophic (2) small lunged or atrophic (3) compensatory (4) acute vesicular and (5) acute interstitial emphysema The last named condition has no relation to true emphysema except in name but will be described in this group for convenience

1 LARGE LUNGED OR HYPERTROPHIC EMPHYSEMA (SUBSTANTIVE OR IDIOPATHIC EMPHYSEMA)

This is a chronic affection and is usually bilateral

Ætiology —*Predisposing causes* —It may occur at any age even in childhood but is most frequently seen in middle and late adult life It is commoner in men than in women probably because they are more exposed to the conditions inducing it Although not strictly hereditary it often shows a familial incidence Certain occupations are credited with being concerned in its production notably those in volving violent or prolonged muscular effort with closed or partially closed glottis such as blowing wind instruments and lifting heavy weights Dusty occupations also favour its onset by leading to bronchitis and cough

The common *exciting cause* seems to be the strain of prolonged and repeated cough induced by chronic bronchitis bronchiectasis asthma whooping cough cigarette smoke inhaling and other causes of irritation of the upper air passages

Pathology —The pathogenesis of emphysema has been much debated and various explanations have been offered (1) Primary degeneration theory Villemin sug gested that the essential lesion was a fatty degeneration of the alveolar walls while Cohnheim believed that there was a congenital defect of the elastic tissue of the lung

is as a rule observed in the morning Hæmorrhage from an enlarged pharyngeal vein is often suggested as a cause but is rarely seen Hæmorrhage after tooth extraction and staining of the mucus expectorated after epistaxis are other causes of spurious hæmoptysis

Pathology —From the list of causes it might be inferred that the origin of the blood differs in different cases It may come from the pulmonary or bronchial vessels in pulmonary tuberculosis and other lung or bronchial conditions, and also in chronic venous congestion or infarction It may come from the thoracic aorta direct or from some of its branches in aneurysm and mediastinal new-growth and from the hepatic vessels in abscess of the liver In cases due to disease of the trachea and larynx it comes direct from the vessels supplying them

Post mortem the larynx trachea and bronchi may contain clots or blood stained froth and mucus and their walls may be stained in places Dark reddish areas of lobular distribution due to inhaled blood may be seen in various parts of the lungs particularly at the bases Sometimes this may induce bronchitic changes described as hæmoptoic bronchitis Careful search in cases of profuse hæmoptysis will usually reveal the source of the hæmorrhage and in pulmonary tuberculosis this is generally a ruptured aneurysmal dilatation in a cavity or an ulcerated vessel The aneurysm may be small and escape notice unless many cuts are made into the lung

Symptoms —In hæmoptysis the patient often experiences a tickling in the throat followed by a gush into the mouth with a salt taste and on expectoration notices blood The alarm and anxiety this occasions lead to restlessness and rapid action of the heart If the bleeding is profuse cough is frequent and large clots together with liquid alkaline blood may be expectorated to the extent of 20 or 30 oz in a few hours The bleeding may cease temporarily to recur at intervals for several days until the patient becomes blanched weak and syncopal with rapid weak pulse In any profuse hæmoptysis death may occur in a few minutes either from asphyxia or syncope In the former case the blood at first bright and arterial is soon dark and frothed while the patient becomes cyanosed and livid In slighter degrees of hæmoptysis there may be only streaks small clots or liquid blood mixed with ordinary sputum After the actual bleeding has ceased the sputum may be blood stained for some days owing to the expectoration of blood inhaled into other parts of the lungs This can be recognised by its colour which varies from dark red to brown owing to the changes undergone by the blood pigment

Diagnosis —This involves two problems—first the differentiation from hæmatemesis and spurious hæmoptysis and secondly the recognition of the cause of the hæmorrhage If the patient is seen at the time of the bleeding the first of these is easy The nature of the blood and its association with cough and possibly with pulmonary or cardiac signs are conclusive When the diagnosis has to be made upon the history given by the patient or by friends it may be difficult especially in the absence of physical signs

In hæmatemesis there is frequently gastric pain and faintness before the vomiting the blood is acid in reaction dark in colour even brown from acid hæmatin and is sometimes mixed with food The fact that in hæmoptysis blood may be swallowed and subsequently vomited increases the difficulty Patients often give very dubious answers to questions as to whether the blood was coughed or vomited up They should then be questioned as to whether sputum was brought up on the following day and if so whether it was blood stained In cases of doubt the investigation of the pulmonary and abdominal physical signs when the patient s condition permits may decide the diagnosis

The utmost caution should be exercised to exclude tuberculosis before making a diagnosis of spurious hæmoptysis Only when there are no pulmonary symptoms signs or radiographic indications and when some obvious cause such as anæmia or pyorrhœa is found is it safe to do so

is common and is to some extent a measure of the degree of emphysema Varying degrees of polycythæmia may be observed The patient may walk about with a more extreme degree of cyanosis than in any other condition except congenital heart disease Clubbing of the fingers of moderate degree is common Cough is usually due to the associated bronchitis and is worse in the winter and in foggy weather It is frequent noisy and often hacking and paroxysmal Expectoration is also the result of the bronchial catarrh and varies from a few grey mucoid pellets to copious muco pus

The chest is enlarged particularly in the antero posterior diameter, the upper thoracic spine is rounded and kyphotic the sternum protrudes forward and the *angle of Louis is prominent the general effect being the so called barrel shaped chest* The ribs run forward more horizontally and the intercostal spaces are wider than normal the chest being as a whole in the inspiratory position The respiratory movements are much restricted the patient elevating the rigid thorax with little expansion on taking a deep breath so that the inspiratory increase at the level of the nipples may be only ½ to 1 inch instead of the normal 2½ to 3 for an adult. There is often filling and even bulging of the supra clavicular hollow while the neck appears short the sternomastoids stand out and the jugular veins are full A zone of dilated *venules the emphysematous girdle is often present along the line of the costal* attachment of the diaphragm but is not pathognomonic The cardiac impulse is not visible as a rule and may only be felt with difficulty, but epigastric pulsation is usually apparent Vocal fremitus is diminished and the percussion note is hyper resonant The superficial cardiac dullness is greatly diminished or even absent and the lower limit of pulmonary resonance may extend to the costal margin back and front the hepatic dullness being encroached on or obliterated

It is said that in bullous emphysema the breath sounds are harsh over the outer part of the upper lobes in front and weak at the bases In general emphysema the breath sounds are weak everywhere inspiration is short and expiration is greatly prolonged A loud rumbling from contraction of the thoracic muscles may entirely obscure the breath sounds A few fine bubbling râles may be heard at the bases or at the sternal margins If bronchitis is present scattered rhonchi may be audible Vocal resonance is generally slightly diminished The heart sounds are weak and distant and in late stages a tricuspid systolic murmur may develop The vital capacity of the lungs measured by a spirometer is often reduced to one half or less Radiographic examination shows increased extent and undue translucency of the lung tissue It shows the diaphragm lower in position and flattened and the costophrenic angle widened The liver is sometimes palpable possibly from down ward displacement by the bulky lung The spleen may also be depressed and palpable

Complications—Bronchitis is the commonest and often causes a vicious circle Asthmatic attacks so called bronchial asthma are common in later stages on the other hand spasmodic asthma may be the cause of the emphysema Pneumo-thorax and interstitial emphysema may occur from rupture of the bullæ although these accidents are relatively rare or perhaps relatively rarely diagnosed since the difficulties of diagnosis in these cases are obvious Pneumothorax is a common com plication of the severe emphysema of advanced pneumoconiosis Pulmonary tuber culosis is an occasional complication of emphysema which contrary to popular opinion is not antagonistic to it although it may mask and obscure the early stages Right sided cardiac failure with its train of consecutive changes is a late and often terminal complication

Diagnosis—This is never difficult in advanced cases The slighter degrees may be more difficult and the diagnosis is then largely a matter of inference from the association of chronic cough and dyspnœa with physical signs of hyper resonance and prolonged expiration

Confusion may occasionally arise with pneumothorax and pulmonary tuberculosis

(2) The inspiratory theory first suggested by Laennec and developed by Gairdner postulates *the force of inspiration as the distending* agent (3) The expiratory theory first enunciated by Mendelssohn was independently brought forward and established by Jenner The distension of the alveoli is regarded as due to the effect of forced expiration and cough Jenner pointed out the special and early involvement of the apices the anterior and lower margins of the lungs in other words the parts least supported by the thoracic cage (4) Freund regarded the changes in the lungs as secondary to calcification of the costal cartilages the chest becoming fixed in the inspiratory position and the lung permanently expanded in consequence Christie in an analysis of these and other theories concludes that there are probably three factors of importance inflation of the lungs caused by obstruction to expiration, loss of elasticity due to the stress and strain of coughing in asthma, lowered resistance of the lung to wear and tear varying from person to person and becoming progressively lower with advancing age

The characteristic conformation of the chest is usually apparent (see Symptoms) the costal cartilages are often calcified and on opening the thorax post mortem the lungs bulge instead of retracting, so that the pericardium may be almost completely obscured They are pale in colour even in town dwellers a condition called albinism of the lung by Virchow They are soft and pit on pressure, and as described by Laennec give the sensation of a down pillow The surface of the lung under the pleura shows a finely vesicular appearance due to the distension of the alveoli the vesicles often being nearly as large as pins heads Not infrequently large bullæ or blister like protuberances, varying in size from a pea to a Spanish olive, occasionally much larger may be seen projecting from the surface particularly at the apices and margins These bullæ when incised show fine fibrous bands crossing them the remains of inter alveolar walls and of atrophied blood vessels It was formerly customary to refer to such cases as bullous or marginal emphysema and to describe those in which the dilatation is less obvious but more widely diffused as general emphysema, but the conditions are so commonly associated together in varying degrees that little is gained by so doing On section the lungs are pale and dry except at the bases where there is frequently some œdema in advanced cases The bronchi may show some general dilatation When bronchitis coexists muco pus can be squeezed from the cross sections of these tubes As pointed out by Fowler pleural adhesion is relatively uncommon The infundibula and alveoli are dilated and the inter alveolar walls are thin and atrophic even disappearing wholly or in part The distension and coalescence of adjacent alveoli result *in the formation* of bullæ The calibre of the pulmonary capillaries is diminished by stretching of the alveolar walls, and where atrophy of the inter alveolar septa occurs the capillaries are destroyed These two processes result in a *considerable diminution* in the total aerating surface and cause the dyspnœa and cyanosis characteristic of the disease Moreover the normal anastomoses between the terminal bronchial and pulmonary capillaries *increase considerably* and *some of the blood in the* latter may therefore fail to reach the alveoli and so escape aeration Atrophic changes in the elastic tissue have been described In order to maintain the circulation through the diminished *capillary area the right ventricle hypertrophies and the resultant* raised blood pressure sometimes induces atheroma of the pulmonary artery Emphysema being a progressive lesion and the defective aeration of the blood perhaps interfering with the *nutrition of the heart muscle* cardiac failure eventually ensues causing tricuspid regurgitation engorgement of the right auricle and the visceral effects of venous engorgement such as ' nutmeg liver

Symptoms —Dyspnœa of varying degree is the most characteristic symptom In uncomplicated cases of moderate extent it is only present on exertion unless bronchitis coexists In advanced emphysema dyspnœa is marked and becomes extreme in the bronchitic or asthmatic attacks and in foggy weather Cyanosis

general atrophy and debility There is shortness of breath only on exertion or on exacerbation of the chronic bronchitis which is frequently present The chest is small flat and thinly covered the movements are poor and there is elevation of the chest as a whole with poor expansion Kountz and Alexander maintain that there is very little diminution in vital capacity that the movements of the diaphragm are increased and that the intervertebral disks are abnormal There is little cyanosis and no clubbing The vocal fremitus is unaltered or slightly diminished The percussion note is hyper resonant but there is no encroachment on the cardiac and hepatic areas of dullness Breath sounds are weak, and there is but little prolongation of expiration Rhonchi and râles may be heard especially if bronchitis is present, or if the heart is failing

Diagnosis—The condition is generally so obvious that no difficulty arises

Treatment—This is chiefly a matter of careful regimen and diet with treatment of co existing bronchitis or cardiac failure

3 COMPENSATORY EMPHYSEMA (LOCALISED OR SECONDARY EMPHYSEMA)

Ætiology—Localised emphysema is a sequel to some process inducing collapse contraction or destruction of areas of lung tissue It may be lobular in distribution in bronchitis broncho pneumonia tuberculosis and diphtheria It may affect one or more lobes or the whole of one lung especially in cases of fibrosis following tuberculosis pneumonia chronic pleural effusion and empyema

Pathology—It is generally conceded that the inspiratory theory of Laennec and Gairdner satisfactorily explains the genesis of this condition When shrinkage of an area of lung occurs the chest wall may fall in if there is pleural adhesion but otherwise inspiration tends to expand the normal parts of the lungs None the less it must be admitted that the expiratory strain of cough may assist in its production

Although it may be compensatory and physiological at its inception it is doubtful whether a true hypertrophy takes place after adolescence In any case it soon leads to atrophy of the alveolar walls as in true emphysema and thus becomes pathological and harmful Post mortem the condition may be found in an upper lobe around contracted scarred lung tissue or in a lower lobe when the upper lobe is contracted or disorganised In cases where one lung is fibroid and contracted compensatory emphysema may be found throughout the sound lung The resulting adaptations caused by enlargement of one part and shrinking of another may produce some striking displacements the lower lobe extending upwards nearly to the clavicle or the anterior margin of the sound lung crossing the mid line The general appearances are closely similar to those of ordinary emphysema except that bullæ do not occur at any rate until the process is advanced and definitely pathological

Symptoms—This condition does not produce symptoms that can be differentiated from those of the primary disease When it affects a lobe or the whole of one lung there is hyper resonance over the area involved which often contrasts strikingly with the dullness due to the primary lesion The hyper resonance may extend across the sternum and even for an inch or more beyond it. The heart is displaced towards the side where fibrosis is in progress Vocal fremitus and vocal resonance are little altered but may be increased at first and subsequently diminished In the early stages when there is alveolar dilatation without degenerative mural changes the breath sounds are exaggerated harsh or puerile but when such processes develop they become weak and there are indications of dyspnœa and cyanosis on exertion

Diagnosis—This is easy owing to the difference between the diseased and compensatory areas and to the indications of contraction and displacement

Treatment—No special treatment apart from that of the primary condition is required

Dr PC ... RAR

Careful record of the symptoms and signs and the investigation of the sputum generally suffice to distinguish these conditions In doubtful cases radiography will assist

Course—Emphysema is progressive unless the cause is removed or the effects of the disease are mitigated by residence in a warm dry climate especially in the winter Conversely, residence in unsuitable districts, persistence in detrimental employment and repeated attacks of bronchitis accelerate its course

Prognosis—This depends upon the degree of emphysema and the circumstances of the patient If progressive it exerts an increasingly crippling effect and it certainly shortens life under urban conditions A '*vital capacity* *of less than 50 per cent* of the normal is of serious import The advent of severe bronchitis or of cardiac complications may affect the prognosis gravely

Treatment—Emphysema may be arrested but cannot be cured Attention must *be directed to prevention of the causes of chronic cough and increased intra alveolar* tension In any person with hereditary tendency to emphysema or to winter cough the questions of occupation and place of residence should be carefully considered When the disease is established, the patient, if in a position to afford it, should spend the winter in a warm more equable climate either abroad or at the south west coast of England

Various attempts have been made to increase the respiratory ventilation of the lungs by deflation The most generally used method is by the use of a well fitting abdominal belt to raise the diaphragm Efforts in the same direction have been made by pneumoperitoneum and even pneumothorax Their justification is doubtful

Expiration breathing exercises are of general application and quite impressive results can be obtained by their use provided the chest wall is not completely rigid Even in these cases diaphragmatic movement can be increased

The diet should be simple and easily digestible especially in the later stages If there is spasmodic dyspnœa or asthma no late meal should be permitted Clothing *should be warm but the excess of under garments often worn in fear* of chill is harmful Patients should avoid those who have colds and should themselves stay in bed at the first sign of such an infection in themselves

In other respects treatment is largely symptomatic In acute bronchitic attacks *the measures to be adopted are in no way different from those in bronchitis un*complicated by emphysema In the more chronic bronchitis so commonly present in the winter iodides with alkalis and balsamic expectorants seem beneficial When asthma or paroxysmal dyspnœa occurs antispasmodic drugs and measures similar to those used in spasmodic asthma may be employed When cardiac failure supervenes the appropriate treatment must be vigorously applied If there is marked cyanosis and venous engorgement oxygen administration and diuretic drugs may be employed, and digitalis administered any associated pulmonary infection even bronchitis requires energetic treatment with the appropriate antibiotic *broncho*spasm should be treated with antispasmodics

2 SMALL LUNGED EMPHYSEMA (ATROPHIC OR SENILE EMPHYSEMA)

Ætiology—This condition occurs in old age and forms part of the general atrophy of the tissues

Pathology—The alveolar walls become thinned and disappear so that adjacent alveoli coalesce The condition is primarily atrophic and therefore differs *from* true emphysema although the result is to produce a diminished area for aeration Post mortem the lungs are small and do not bulge or obscure the pericardium They are often deeply pigmented and are more spongy than normal but although bullæ occur they are small On section the lung tissue is bloodless and friable *The bronchi* may be slightly dilated and show catarrhal changes

Symptoms—These are slight and are masked by the enfeeblement due to the

septic processes such as otitis media and infective thrombo phlebitis Amœbic abscess occurs occasionally after dysentery and pulmonary abscess may be found as a rare complication of enteric fever (4) From infection of the lung tissue due to spread from adjacent disease This may occur in bronchiectasis in ulcerating new growths of the lung bronchi, œsophagus or mediastinal glands in caries of the vertebræ or ribs, and in suppurating mediastinal glands Rupture of an empyema, of a subphrenic abscess of a liver abscess or of infected hydatid cysts of the lung or liver may also lead to pulmonary suppuration Ten per cent of cases of abscess are due to new growths (5) As a sequel of perforating chest wounds or of fractured ribs piercing the lung

Pathology—Abscess of the lung is generally single and basic when consequent on pneumonia whereas embolic abscesses are often small and multiple and may be found in any part of the lung Abscesses due to extension from adjacent disease are generally solitary, and are often large and irregular The walls of acute abscesses are generally formed of congested and œdematous lung tissue, or of a zone of un resolved pneumonia Since acute abscesses commonly rupture quickly into a bronchus a fibrous capsule is unusual but in chronic abscess there is often considerable fibroid change in the neighbouring lung tissue The pleura may become involved over superficial abscesses leading to empyema or to pyo pneumothorax if rupture follows

Symptoms—Abscess may develop insidiously with comparatively slight symp toms More commonly they are an intensification of those due to the primary or antecedent condition The patient often appears seriously ill the fever becomes of septic type remittent or intermittent in character and of a high range Rigors and sweating are common Clubbed fingers are a characteristic and early sign The pulmonary symptoms at first may be only slight cough with scanty muco purulent expectoration Dyspnœa may be present and pain of acute character develops if the pleura is involved Hæmoptysis occurs in 70 per cent of cases of abscess A considerable leucocytosis up to 20 000 or 30 000 may be found and occasionally the breath may be offensive even before rupture into a bronchus occurs followed by the sudden expectoration of a large quantity of pus The pus is sometimes unpleasant or offensive smelling but has not the extreme fetor of gangrene Microscopical investigation will demonstrate the presence of pulmonary debris especially elastic tissue together with pus cells and micro-organisms After the expectoration of the pus the temperature usually falls and the general condition of the patient is much improved though cough and expectoration persist In chronic cases after rupture the temperature may become irregular and periodic a few days of normal temperature being followed by a period of fever and later by increased expectoration The physical signs in a deep seated or small abscess are often inconspicuous and comprise slight dullness over a small area weak breath sounds and possibly a few rales in the surround ing infiltrated or œdematous lung tissue With a large or a superficial abscess the signs before rupture may be those of consolidated or collapsed lung After evacuation occurs the characteristic signs of excavation usually develop at once In multiple embolic abscesses the signs are usually those of disseminated broncho pneumonia and in multiple abscesses due to staphylococcal infection widespread diffuse opacities may be apparent on radiographic examination These rapidly develop into cavities either empty or with a fluid level They may be mistaken for lung cysts owing to their thin walls

Complications and Sequelæ—The commonest complication is dry pleurisy This may progress to empyema or to pyo pneumothorax if rupture into the pleura occurs In some cases mediastinitis or pericarditis may develop Gangrene is de scribed but is a rare sequel Metastatic abscesses may be produced in other parts of the body especially in the brain and meningitis is a rare and serious complication The most important sequelæ are fibrosis of the lung with bronchiectasis pleural adhesion and rarely indurative mediastinitis

4 ACUTE VESICULAR EMPHYSEMA

Although custom has included this condition with emphysema, it is in reality *only a temporary* acute distension of the alveoli resulting from any condition causing widespread obstruction of the smaller bronchi It is sometimes observed after death in cases of acute bronchitis, whooping cough or asphyxia and in anaphylactic shock, and its existence may be inferred in severe asthma Post mortem the lungs are bulky and the alveoli distended

The symptoms are dependent upon the primary condition, although dyspnœa is invariably present The chest is found to be fully expanded, the vocal fremitus is diminished the percussion note is hyper resonant and the breath sounds vary with the condition inducing it In cases due to asthma the injection of a few minims of $\frac{1}{1000}$ adrenaline often produces visible deflation and helps to differentiate it from hypertrophic emphysema

5 ACUTE INTERSTITIAL EMPHYSEMA

In acute interstitial emphysema air is present in the stroma of the lungs and in the subpleural connective tissues It may follow external trauma such as fractured ribs, or wounds penetrating the lungs The alveoli may rupture with violent expiratory efforts as occur in whooping cough or influenzal broncho pneumonia It may occur in diphtheria The air sometimes tracks along the pulmonary roots to the mediastinum, and appearing in the neck or on the chest wall gives rise to surgical emphysema

Post mortem, subpleural bullæ may be seen containing air and on section of the lung minute air bubbles may be found in the inter alveolar connective tissue A diagnosis cannot be made unless the physical signs of surgical emphysema are present. The air is usually completely absorbed and a perfect recovery takes place No special treatment is required beyond keeping the patient at rest and giving sedative drugs to allay cough

ABSCESS OF THE LUNG

Definition —Abscess of the lung includes any circumscribed collection of pus ormed in the lung tissue but softened tuberculous areas and bronchiectatic accumulations are usually excluded

Ætiology —*Predisposing causes* —These include any diseases producing general cachexia or malnutrition notably diabetes and chronic alcoholism also any conditions leading to diminished resistance locally in the lung such as injury disease or exposure

Exciting causes —These are pyogenic organisms which reach the lung by inhalation by extension from adjacent suppurative processes or by the blood stream either directly or in septic emboli The common organisms found are streptococci staphylococci the pneumococcus, Friedlander s pneumo bacillus *Cl welchii* and *Bact coli*—sometimes acting in conjunction with putrefactive bacteria Spirochætes *F fusiformis* and other anaerobic organisms are often present especially after rupture has occurred Pulmonary abscess may form under the following conditions

(1) After inhalation of foreign material into a bronchus This may be a foreign body or may occur in association with septic conditions in the nose naso pharynx and larynx or during and after operations in these regions These are referred to as inhalation abscesses though some post-operative cases are regarded as due to embolism and not to inhalation (2) As a result of lobar or lobular pneumonia especially after the deglutition and aspiration varieties of the latter Such abscesses are sometimes called meta pneumonic (3) Embolic cau es—in pyæmia, or following on septic pulmonary emboli due to right sided septic endocarditis or derived from distant

In a considerable number of cases recovery takes place with penicillin and postural drainage alone

If in spite of postural drainage and the use of suitable antibiotics there is no steady progress of improvement from week to week surgical intervention is called for The operation of choice in these cases used to be external drainage after the sealing off of the pleura Resection however is more effective when the localisation of the abscess renders the procedure possible

Bronchoscopic drainage has its advocates and its successes but it has little advantage if any over postural drainage except that it is sometimes successful by making the patient cough Artificial pneumothorax is never advisable in these cases owing to the imminent danger of pyo pneumothorax

GANGRENE OF THE LUNG

In this condition localised or diffuse areas of lung tissue undergo putrefactive necrosis

Ætiology —*Predisposing causes* —These include old age over indulgence in alcohol general debility diabetes and insanity In certain rare cases especially after broncho pneumonia complicating measles gangrene of the lung is met with in children

Exciting causes and associated conditions —These are in the main identical with those of pulmonary abscess (see p 1002) In addition the pressure of aneurysm or of new growth on branches of the pulmonary artery may lead to gangrene The causal organisms are also very similar to those found in abscess of the lung and include staphylococci streptococci sarcinæ the *Micrococcus tetragenus Bact coli Ps pyocyanea F fusiformis* with its associated spirochæte and various anaerobes Some of these organisms yield putrefactive products with the liberation of phenol indole and skatole compounds

Pathology —It is not quite clear what are the factors determining whether abscess or gangrene occurs in an infected area of lung Doubtless the general resistance of the body the degree of local vascular disturbance and the virulence of the infecting organisms all play their part Laennec first described the two varieties of gangrene the circumscribed and the spreading or diffuse Around the former there are indications of a line of demarcation formed by congested lung tissue which may present the appearance of red hepatisation The surrounding lung tissue is invariably somewhat œdematous The gangrenous area is soft and pulpy and its colour varies from reddish brown to greenish black As the necrosis advances putrefactive liquefaction occurs with the formation of a horribly reeking fluid containing shreds and masses of necrotic lung tissue When this is discharged excavation results and isolated vessels may be seen running across the resulting cavity the walls of which are rough and covered with fetid pus The diffuse variety of gangrene is less common there is no attempt at a zone of demarcation and the whole of a lobe or of one lung may be affected In both forms the overlying pleura is intensely inflamed and empyema or pyo pneumothorax may be produced

Symptoms —These are similar to those occurring in abscess of the lung but are more acute The patient is desperately ill rigors are more common and sweating is more profuse The breath has a peculiar fetor which on account of the presence of the skatole group of putrefactive products in the gangrenous lung has an almost fæcal odour The sputum is intensely offensive and on standing separates into three layers similar to those of the expectoration in cases of bronchiectasis Elastic tissue is usually present Hæmoptysis is not infrequent and may prove fatal In rare cases gangrene is not accompanied by fetid expectoration especially when developing in the insane in young children and in diabetics or after pulmonary embolism

Diagnosis —This is difficult before rupture into a bronchus but abscess may be suspected from the gravity of the symptoms in relation to the history and signs especially if leucocytosis and fetor of the breath are present Radiographic examination may be helpful by demonstrating a localised shadow before rupture and excavation afterwards and also by establishing the situation of the abscess A fluid level can often be seen in films taken in the erect position although a fluid level may sometimes be more obvious if the patient is radiographed lying on one or other side or tilted to one side The sudden expectoration of pus followed by retrogression of symptoms and signs of excavation is very suggestive of abscess After rupture has occurred the differential diagnosis has to be considered from

1 *Interlobar empyema* —This may be very difficult or even impossible In this condition the signs are generally most marked in the region of an interlobar septum there may be some cardiac displacement, and the sputum, though purulent, does not contain elastic tissue

2 *Bronchiectasis* —The history the characteristic cough and sputum and the variation of the physical signs with the state of the cavity usually suffice to distinguish this condition A lipiodol or Neo Hydriol bronchogram will distinguish in doubtful cases since the oil does not as a rule, enter abscess cavities and the appearances in bronchiectasis are characteristic

3 *Gangrene of the lung* —This is a distinction with little difference except that gangrene is a suppuration of the lung that has not localised The extreme gravity of the patient s general condition and the horrible fetor of the breath and sputum are the most characteristic features of gangrene

4 *Tuberculous excavation* —The history, the distribution of the signs and the characters of the sputum including the presence of tubercle bacilli, are the distin guishing indications

5 *Purulent bronchitis* —The history the widespread physical signs and the absence of elastic tissue from the sputum usually serve to establish the diagnosis and lipiodol or Neo Hydriol investigations may be helpful

In multiple or pyæmic abscesses it is often impossible to recognise the condition though it may be suspected from the severity of the symptoms and signs In any doubtful case radiographic examination or tomography should be carried out if the condition of the patient permits The possibility of malignant growth as a cause of abscess should be borne in mind and when necessary bronchoscopy as well as lipiodol investigation carried out Exploratory puncture as a means of diagnosis is dangerous and should be avoided

Prognosis —The prognosis though grave in many cases is better than might be anticipated and has been much improved by modern treatment Pyæmic abscesses have a more serious prognosis except when staphylococcal which sometimes improved spontaneously even before the days of antibiotics

Treatment —Penicillin should be given in doses of 1 to 2 million units daily as soon as the diagnosis is made When sputum from the abscess is available the sensitivity of the various organisms should be tested in case any of them are penicillin resistant but are sensitive to streptomycin chloramphenicol, chlortetracycline or other antibiotics A careful record of the daily amount of sputum must be started and the patient given postural drainage in the position appropriate to the site of the abscess

The posturing must be kept up for as prolonged periods as possible Special beds on frames make prolonged postural drainage more effective and more comfort able Tapotage over the abscess in the correct postural position helps drainage of the abscess and breathing exercises should be combined with the postural drainage Once the abscess has started to discharge diminution in the measured amount of sputum should be accompanied by improvement in the clinical condition If it is not the drainage is imperfect Improvement must be correlated with radiological changes

of a bronchus and leading either to collapse or to bronchiectasis may if long continued cause fibrosis of the corresponding lung area Among such may be mentioned inhaled foreign body new growth cicatricial contraction and thoracic aneurysm

Pathology —The fibroid overgrowth may be (1) Massive or lobar (2) localised or insular (3) peri bronchial and (4) reticular

Any part of the connective tissue framework of the lungs and bronchi may contribute to the fibrosis In the massive form which generally affects the whole or the major part of a lobe or even of one lung the appearances in cases due to tuberculosis differ from those due to other causes In the tuberculous variety the primary distribution is usually apical and evidence of other tuberculous processes may be apparent in the form of large or small dried up cavities inspissated caseous material or calcareous masses enclosed in fibrous strands In non tuberculous processes the early localisation is commonly basal and although the primary cause may be obvious in the form of bronchial obstruction or some pleural condition this is not always the case On the other hand non tuberculous processes may involve the upper lobe primarily and fibroid tuberculosis may fall with special stress upon the lower lobe In both forms of fibrosis bronchiectasis may result although this is more common in the non tuberculous cases Apart from the special tuberculous lesions the end-results are very similar in both forms The affected area of the lung is shrunken and often devoid of air except for that in the bronchi and in the cavities It is dark in colour very firm and hard On section it presents a mottled appearance owing to the strands of blue grey fibrous tissue traversing it contrasting with the pigmented condensed airless lung tissue The fibroid area may be honeycombed by cavities or may present one large excavation due either to tuberculous cavitation or to bronchiectatic dilatation There is nearly always thickening and adhesion of the pleura The contraction of the abnormal fibrous tissue leads to marked displacement of the heart and mediastinum

The localised form is commonly due to healed tuberculous processes at an apex There may be simple puckering with or without pleural thickening and adhesion or a dense mass enclosing dried up caseous matter or calcareous spicules In bronchitic or broncho pneumonic processes a patchy fibrosis may occur described as insular fibrosis by Fowler

Reticular fibrosis is a rare condition in which the fibrous tissue in the interlobular septa seems to become increased as well as that around the bronchi It is at present only of pathological interest

Symptoms —The symptoms of pulmonary fibrosis are in the main expectoration and dyspnœa together with those of the primary affection In the non tuberculous cases bronchiectasis is so frequently associated that the symptoms and signs found are practically those of this condition Even in tuberculous cases some degree of bronchial dilatation is the rule although the sputum is rarely offensive The cough is generally periodic and associated with change of posture The expectoration is abundant and if bronchiectasis is present it has the usual characteristic features The dyspnœa is proportional to the extent of lung involved It may be extreme in the later stages when the heart becomes embarrassed and begins to fail Fever is usually absent except when complications occur

The patients are generally spare although nutrition may sometimes be well maintained until late They may show signs of deficient aeration in duskiness cyanosis and congested cheeks Polycythæmia sometimes occurs Clubbing of the fingers is almost constant Evidence of contraction is generally forthcoming in the flattening and retraction of the affected side with the dropped shoulder and compensatory spinal curvature Movement is greatly restricted contrasting with the increased expansion of the other side The cardiac impulse is sometimes much displaced especially in left sided cases when it may be in the left posterior axillary line or even under the angle of the scapula In right sided cases it is drawn to the right of the

The physical signs closely resemble those present in cases of pulmonary absce s and are those of consolidation before liquefaction occurs and of excavation afterwards The signs of the antecedent condition such as bronchiectasis aneurysm or malignant *disease may also be* present

Complications and Sequelæ—These are similar to *those met with in pul* monary abscess, but owing to the rapid course and greater fatality of gangrene they are not so common Cerebral abscess may occur

Diagnosis—The differential diagnosis is as for pulmonary abscess the dis tinguishing features being the extremely critical condition of the patient and the revolting fetor of the breath and expectoration Radiographic examination may give great assistance if the patient's condition permits it to be made

Course—The course is usually rapid, unless the diseased area is small and circumscribed In rare cases of localised gangrene of small extent, resolution and subsequent fibrosis occur

Prognosis—This is always *extremely grave, though a few cases of* localised gangrene recover spontaneously The prognosis is improved by early operation in suitable cases The outlook is said to be worse if the condition is apical, and diffuse gangrene is invariably fatal

Treatment—Operation is indicated when the general condition of the patient permits if the gangrenous area can be localised by physical signs or radiographic examination Exploratory puncture should not be carried out The other operative procedures are similar to those for abscess of the lung Operation is contraindicated in cases of diffuse gangrene The medical treatment is in all respects similar to that for pulmonary abscess Injections of neo arsphenamine, in doses of 0 3 g have given good results especially in cases due to fuso spirochætosis The sensitivity of the organisms in the sputum to the various antibiotics should be determined and the appropriate antibiotic given

PULMONARY FIBROSIS

Synonyms—Fibroid Disease of the Lung Chronic Interstitial Pneumonia Cirrhosis of the Lung

Definition—Pulmonary fibrosis is a late sequel of many acute and chronic inflammatory or irritative processes affecting the bronchi lungs and pleuræ It is therefore rather of pathological than of clinical interest and in no sense constitutes a separate disease, although the end results are remarkably similar in different forms *It is described here partly in deference to tradition and partly* to point out the methods of diagnosis between the various causes producing such strikingly similar effects

Ætiology—(1) The commonest cause is pulmonary tuberculosis particularly the fibroid and fibro caseous varieties (2) The group of pneumoconioses contributes a considerable number of cases *and possibly some varieties of* gas poisoning may induce fibroid changes (3) Broncho pneumonic processes particularly the forms associated with measles and whooping cough may be followed by widespread fibrosis especially in children (4) Although fibroid induration is commonly described as a sequel of lobar pneumonia *this disease is one of the rarer causes* (5) Localised fibrosis may occur around any circumscribed pulmonary or bronchial lesion such as that produced by syphilis leprosy glanders or actinomycosis Similarly it occurs about infarcts pulmonary abscesses and parasitic cysts (6) Chronic venous con gestion if prolonged leads to fibroid change which is referred to as brown indura tion This is usually of moderate degree and does not affect the clinical manifesta tions (7) Chronic pleural affections particularly those leading to adhesions or causing pulmonary collapse may induce fibroid changes within the lung and these forms are described as pleurogenous cirrhosis (8) *Any condition* causing obstruction

Nature of dusts —Dusts consist of particles or aggregates of particles suspended in air and measuring from 150 microns to 0 5 microns in diameter The sand of deserts the dust of streets and the pollens of plants are of such large particle size that they become trapped in the nose and upper respiratory passages and never reach the lungs Industrial dusts result from vigorous mechanical attrition blasting grinding drilling rubbing crushing hammering and sawing Particles 5 microns or less in diameter *can reach the alveoli of the lungs in the ashed lung specimens of men who have* died of silicosis the most representative particle measures 1 micron in diameter

Reaction of lung tissue to dusts —Of the dusts which do reach the alveoli silica and fibrous silicates set up different types of fibrous reaction in the lungs and the process is usually progressive But the dusts of some of the non fibrous silicates and of the compounds of certain metals among them calcium iron tin and barium seem to be inert when inhaled They are capable of lying in the lungs for years without inducing any deposition of fibrous tissue or other reaction but because they are relatively radio opaque they may produce changes in the X ray film which must then be distinguished from those of silicosis The resulting conditions are sometimes referred to as *benign pneumoconioses* The inhalation of vegetable and animal dusts may cause asthma and bronchitis indistinguishable from these diseases of non occupational origin

I SILICOSIS

Synonyms —Dust Consumption Ganister Disease Grinders Asthma Grinders Consumption Grinders Rot Grit Consumption Masons Disease Miners Asthma Miners Phthisis Potters Rot Rock Tuberculosis Stone Hewers Phthisis and Stonemasons Disease

Definition —A disease due to the inhalation of uncombined silica (silicon dioxide) Silicosis and pneumoconiosis must not be used as synonymous terms Logically one could classify the pneumoconioses as pneumoconiosis due to silica pneumo coniosis due to asbestos pneumoconiosis of coal miners and so on but such a method would be too cumbersome Legal considerations make it important that the term silicosis be reserved for that condition caused by the inhalation of uncombined silica the special characters of which render it capable of being identified when it occurs in typical form Dusts other than uncombined silica produce pneumoconioses but these do not present the characters which are possessed by silicosis in its typical form

Ætiology —The industries of sandstone quarrying mining and dressing are the most widespread of all silicosis producing industries in Great Britain In various parts of the world the granite industry the mining of gold hæmatite iron ore tin and coal sandblasting and the manufacture of refractory materials produce cases of silicosis The severity of the disease depends on such factors as duration and intensity of exposure dust particle size and to a large extent on individual susceptibility The *solubility theory* of its causation supposes that the fine particles of stone dust which get into the lungs are pathogenic not because they produce microscopic trauma but because a toxic substance dissolves from their surfaces This is thought to be silicic acid It has also been suggested that the role of silicic acid in silicotic tissue depends on its degree of polymerisation and that only highly polymerised silicic acids are capable of producing fibrosis

Pathology —Round nodules of fibrous tissue 2 to 5 mm in diameter are scattered throughout the lungs Several may be aggregated together to form large composite nodules or they may be united in a massive fibrosis Individual nodules may be thrown into sharp relief by emphysema of the surrounding lung and their centres sometimes undergo calcareous change Histologically the silicotic nodule is a mass of concentrically laminated dense fibrous tissue and similar changes are found in

sternum even sometimes under or outside the right nipple Vocal fremitus is either increased or diminished depending on the patency of the bronchus and percussion gives dullness of varying degree over the fibroid area, while the unaffected parts may be hyper resonant from compensatory' emphysema The diaphragm may be drawn up, and the liver or stomach correspondingly displaced The breath sound may be weak or inaudible but often when a deep breath is taken bronchial breathing can be heard especially if there is underlying bronchiectasis If there is cavitation the breathing will be cavernous or amphoric The presence of whispering pectoriloquy is an important indication that bronchial breathing will probably be heard Vocal resonance will be increased where the breath sounds are bronchial or diminished if the bronchi are not patent Adventitious sounds may be entirely absent and when present vary from rhonchi and bubbling râles to coarse metallic râles according to the presence or absence of excavation Radiographic examination gives useful confirmation showing contraction of the rib spaces scoliosis of the spine to the opposite side displacement of the trachea and heart to the side of the opacity in which translucent areas of cavitation may be seen occasionally

Diagnosis —The diagnosis is usually easy The evidence of contraction and of *mediastinal displacement towards the affected side especially if signs of cavitation* are also present is highly suggestive In the absence of the cavitation some difficulty may arise in regard to chronic pleural effusion or empyema In the earlier stages the contra lateral displacement of the cardiac impulse should prevent any mistake but where partial absorption has occurred, this may be very slight or absent In such cases an exploratory puncture or a radiographic examination may be helpful

When the diagnosis of pulmonary fibrosis has been made the differentiation of the cause is an essential to prognosis and treatment If the condition is apical there is a presumption in favour of tuberculosis if basal some other cause is more probable Repeated examinations of the sputum should be made for tubercle *bacilli* and if these prove negative radiographic examination may reveal some cause such as new growth aneurysm or even foreign body In some cases a careful consideration of the history may afford a clue to the diagnosis

Course —*The course is invariably chronic* and may not shorten the natural span of years

Prognosis and Treatment —These depend upon the primary condition but in most cases the latter is mainly symptomatic

R A YOUNG
G E BEAUMONT
E R BOLAND

THE PNEUMOCONIOSES

Definition —A group of lung diseases which result from the inhalation of dust in various trades Strictly they should be called *Pneumonokoniosis*

Classification —The pneumoconioses can be considered under headings according to the nature of the dust involved

1 Silica
2 Coal
3 Fibrous silicates
4 Non fibrous silicates
5 Non pathogenic inorganic dusts
6 Pathogenic inorganic dusts
7 Vegetable dusts
8 Animal dusts

exhaust ventilation must be used in such an occupation Where castings and other metal objects are cleaned by sandblasting the man wears a special dress so arranged that he breathes pure air from outside the sandblasting cabinet It is better to use shot blasting in which crushed ball bearings replace sand The steel powder resulting is harmless The hydro blast is the safest apparatus used to clean castings A high velocity jet of sand and water is projected on to castings thereby removing moulding material cores and scale The velocity of the water as it leaves the hydro blast gun is in excess of 3 miles per minute In all these trades where it is found impossible to control the dust completely the worker must wear either a dust mask or an air line breathing apparatus

Pre employment clinical and radiographic examinations of the chest are essential Periodical radiographic examinations enable silicosis to be detected at an early stage They therefore help to get men out of a dusty industry before damage to the lungs has gone too far They are also a means of discovering men with pulmonary tuberculosis who not only expose themselves to additional risk by remaining in the dusty occupation but are possible sources of infection to their fellow workers

2 PNEUMOCONIOSIS OF COAL MINERS

Synonyms—Pneumoconiosis of Coal Workers Coal Miners Asthma

Definition—A dust disease of coal workers slowly disabling and quite different from classical silicosis The rise in its incidence particularly in South Wales since 1925 can be related to the great increase in the amount of dust which has followed the mechanisation of the industry

Ætiology—The bulk of cases occurs in colliers working at the coal face and to a less extent among other underground workers That the disease is also found in surface workers on the screens and in coal trimmers at the docks strongly suggests that the causative agent is coal dust and not silica Classical silicosis occurs in only the small percentage of coal miners who are exposed to silica dust in the occupations of ripping brushing driving a hard heading and driving a cross measure drift but both coal pneumoconiosis and silicosis are often indistinguishably combined The highest incidence of the disease is found in the mining of high rank coal or anthracite it is less common in medium rank or steam coal mines and least common in low rank or bituminous coal mines

Pathology—Throughout the lungs coal dust collects in foci around the small bronchioles and their accompanying arteries and a diffuse network of reticulin fibres is laid down around these foci In certain cases the air spaces around the coal foci become dilated an appearance described as *focal emphysema* these emphysematous spaces may enlarge and become confluent although bullæ projecting from the surface of the lung do not occur In other cases a progressive coalescent collagenous fibrosis occurs leading to the formation of nodules and later to a massive fibrosis This fibrosis may be due to a sporadic factor such as silica with possibly a complicating tuberculosis infection In some cases the changes of tuberculosis predominate

Symptoms—The clinical course of the illness may cover many years and routine radiographic examinations usually show changes in the lungs before the onset of symptoms Dyspnœa and cough productive of coal black sputum are the most prominent the chest becomes emphysematous and there may be clubbing of the fingers The earliest radiographic change is a fine network of pinhead shadows sometimes sharp and lace like but much more often blurred Such shadows are variously known as *reticulation* or *pinhead mottling* They are followed by the stage of *nodulation* where the nodules are 2 to 5 mm in diameter The next stage is one of coalescent nodulation and in more advanced cases there are multiple less well defined fluffy shadows Large well defined dense massive shadows are seen in advanced cases of *progressive massive fibrosis* Focal emphysema cannot be diagnosed in life but its

the tracheo bronchial lymph glands Tuberculosis often complicates silicosis and the pathological appearances of the one may obscure those of the other

Symptoms—There is usually a history of exposure to silica dust of about 30 years duration but the latent interval is extremely variable, varying from 6 months to 60 years and the patient has on occasion left the industry for some years before beginning to complain

Silicosis is generally divided into first second and third stages, or slight moderate and severe degrees The first stage the so called simple silicosis supervenes in a workman who has been employed in an industrial process involving exposure to siliceous dusts for a period of many years The onset of symptoms is marked by dyspnœa on exertion slight at first and later increasing in severity Throughout the illness dyspnœa remains the most important symptom Slight cough may be present from the first It is usually unproductive or with scanty sputum The general condition of the patient is unimpaired Physical signs in the chest are slight. Diminished expansion is scarcely if at all present Dullness can rarely be demonstrated and in older subjects there may be areas of hyperresonance due to emphysema There is no alteration of the breath sounds and there are no added sounds In this early stage the radiograph shows the presence of discrete nodular shadows circular and at the most 2 mm in diameter They may be partially distributed throughout the films more widespread or even generalised but they remain discrete In this stage, impairment of working capacity may be slight or absent

In the second stage dyspnœa and cough become established and further physical signs appear There is diminished expansion of the chest patchy dullness sometimes with bronchial breath sounds and scattered rhonchi, especially at the bases The radiograph shows the whole of both lung fields occupied by shadows indicative of nodulation and there is some coalescence to form more or less dense opacities There is always some degree of impairment of working capacity In the third stage dyspnœa leads to total incapacity The radiographs indicate areas of massive consolidation Right heart hypertrophy and then failure may supervene Pulmonary tuberculosis may be present in any stage of silicosis It may alter the symptoms, physical signs radiographic appearances and the whole course of the disease It is the most frequent accompaniment of silicosis Since tuberculosis of the lungs may simulate silicosis in radiographs no diagnosis should ever be made exclusively on radiographic appearances

Treatment—Silicosis is a man made disease and should be prevented In mining operations ample dilution of the air in the mine with fresh air is the simplest method of reducing the dust concentration Various forms of ventilation are in use Drilling with pneumatic hammer drills is responsible for much dust but usually wet drilling can be employed The method used consists of hollow drill steels through which a continuous spray of water passes After shot firing a mist projector is used to allay dust It is really an atomiser using compressed air and spraying a mixture of water containing 0 5 per cent of castor oil In order to avoid the hazard of dust inhalation no man is allowed to return to the rock face until 8 hours after the blasting charges have been fired

In the grinding trades sandstone wheels should be abolished and replaced by wheels made of harmless synthetic abrasives such as carborundum (silicon carbide) and corundum (aluminium oxide) Where sandstone wheels are still used the operations of rodding and hacking as well as the actual grinding of metals must be carried out under a continuous stream of water which is drawn away from a trough at the base of the rotating grindstone

In foundries steel and other metals are poured in the molten state into sand moulds and it follows that the final castings are partly covered with sand and therefore can produce silica dust when treated with particular tools Fettling (steel dressing) implies the use of a compressed air chisel to clean up a casting Locally applied

The radiograph shows a diffuse ground glass or fine cobweb appearance, mainly at the lung bases It changes later into a fine punctate stippling and extends to involve the middle and upper zones although the extreme apices usually remain unaffected The interlobar pleura is thickened and there is a shaggy appearance to the heart outline

Prognosis—Fibrosis develops more rapidly than in the case of silicosis and death may occur within 5 years of the onset of symptoms The incidence of associated pulmonary tuberculosis although not as high as in silicosis is significant Bronchial carcinoma supervenes in more than 10 per cent of cases

Treatment—Treatment is symptomatic only In asbestos mining wet rock drilling is imperative In factories and textile mills the principle of locally applied exhaust ventilation must be enforced to prevent the escape of asbestos dust into the air of any room in which work is done Suppression of dust in the cleaning of carding machines is best ensured by the use of a revolving brush fitted with a cover and connected to a portable vacuum cleaner By the use of closed in machines handling should be reduced to a minimum Dust washes must be used where necessary In Great Britain legislation has been so effective in controlling the disease that with few exceptions cases now diagnosed have industrial histories going back before 1931

(b) TALCOSIS

Talc is a hydrated magnesium silicate It is used as a toilet powder as a dusting agent for rubber tyres and gloves in ceramics and in the manufacture of paper Talc pneumoconiosis has occurred mostly in the mining and milling industry Disability is less than might be suggested by the radiographic appearance of nodular shadows distributed diffusely over both lung fields There is however an increased susceptibility to pulmonary tuberculosis

(c) SILLIMANITE PNEUMOCONIOSIS

The sillimanite group of minerals are all aluminium silicates and are used in the manufacture of high grade refractories Radiographic and histological changes have been found in workers exposed to the dust although there is no disability

(d) SERICITE PNEUMOCONIOSIS

Sericite which is a fibrous variety of muscovite has without justification been suggested as a cause of pulmonary disease The fibre particles are too small to produce the sort of reaction which is found in asbestosis they are however often present in the lungs of miners with silicosis because of the association of sericite with quartz

4 NON FIBROUS SILICATES

The minerals in this group are complex aluminium silicates combined with potassium magnesium or iron When inhaled as dusts they cause no disability but are capable of producing the radiographic changes of pneumoconiosis

(a) MICA

Mica is transparent and heat resistant and is therefore used for the chimneys of oil lamps and for peep holes in furnaces and stoves Because of its high resistance

presence may be suspected when there is intense dyspnœa leading to death from respiratory or right heart failure Where the changes are those of massive fibrosis, progression is less rapid unless active pulmonary tuberculosis unresponsive to treatment, supervenes The course of pulmonary tuberculosis is generally modified by coal pneumoconiosis and often its presence cannot be identified confidently in life This is in contrast with the severe type of infection which occurs in patients with silicosis Thus in coal pneumoconiosis the miner is more breathless than ill and dies of *miners' asthma* whereas in silico tuberculosis he is ill as well as breathless and dies of *miners phthisis*

Treatment —As in the case of silicosis treatment is entirely symptomatic Young men with quite advanced simple pneumoconiosis are usually not seriously disabled whereas men with progressive massive fibrosis are much disabled and their disability increases both with age and with deterioration in radiographic appearances It has been shown that simple pneumoconiosis does not progress in the absence of further exposure to coal dust, whereas massive fibrosis is nearly always progressive whether or not dust exposure ceases This is a strong argument in favour of periodic radiographic examinations Measures directed towards dust suppression are wet cutting wet drilling water infusion of the coal face and hand spraying of the coal face before the coal is pulled down Adequate ventilation is of course essential in reducing dust concentration

3 FIBROUS SILICATES

The fibrous silicates include asbestos talc, sillimanite and sericite

(a) ASBESTOSIS

Ætiology —Asbestos is the name given to a series of minerals composed of the silicates of magnesium and iron crystallised in silky and fibrous form Canada produces 65 per cent of the world s asbestos It is mined both in open pits and by underground methods In Great Britain the main processes involved in the asbestos industry include the crushing and disintegration of the raw material carding and card cleaning and finally the spinning of the yarn and weaving of the cloth Besides being woven, asbestos is ground and mixed with cement and plastics to make insulating slabs and many other articles Asbestosis can follow employment in any of these processes but the risk is greatest in the crushing disintegrating carding and card cleaning processes where there is most dust It seems that the fibrosis is caused by mechanical irritation from the asbestos fibres during the movements of respiration and that this peculiarity is related to the flexibility of the fibres not possessed by other foreign bodies

Pathology —Large areas of the lung are tough owing to the presence of fibrous tissue emphysema although extensive is usually localised to the lower and apical parts of the lungs and there are many pleural adhesions On histological examination the alveolar walls are diffusely thickened there is generalised fibrosis and throughout the lung tissue are seen fibres of asbestos and asbestosis bodies

Symptoms —The average length of exposure before the onset of symptoms is 7 years Dyspnœa is the most conspicuous symptom and it may be out of proportion to the signs found in the chest There is often a non productive cough with pain between or under the shoulders and behind the sternum but hæmoptysis does not occur except in the presence of pulmonary tuberculosis Clubbing of the fingers is not uncommon examination of the chest shows limitation of respiratory excursion sometimes with medium crepitations of a metallic tone in both bases Asbestos bodies are found in the sputum These are golden yellow structures of beadlike form elongated and often with bulbous ends and varying in length from 20 to over 200 microns An asbestos fibre forms the central core in the body

(b) PNEUMOCONIOSIS IN BAUXITE SMELTERS (SHAVER S DISEASE)

Between 1941 and 1943 *aluminosis* occurred at Niagara in men exposed to fume in the manufacture of the abrasive corundum (Al_2O_3) a form of artificial emery They heated bauxite an ore containing 80 per cent Al_2O_3 and up to 7 per cent SiO_2, with iron and coke in the electric ore at 2000 C Some of the bin men furnace feeders and overhead crane men developed diffuse fibrosis of the lungs with emphysematous bullæ but without silicotic nodules There were 13 deaths from pneumothorax. One man had 8 pneumothoraces and he is the only man seriously affected who still lives Meanwhile tuberculosis has not developed in the lungs of the survivors

7 VEGETABLE DUSTS

Chronic lung disease sometimes results from the prolonged inhalation of the dusts of bagasse cotton derris flax flour gum arabic grain hay hemp jute linseed malt, nuts paprika sisal straw, tea and wood It usually takes the form of chronic bronchitis indistinguishable from non occupational bronchitis and it is not accompanied by any characteristic radiographic appearance

(a) COTTON

Four conditions affecting the respiratory system are described in workers exposed to cotton dust in different parts of the world These are mill fever byssinosis weavers cough and an acute illness occurring among people who handle low grade stained cotton

(1) *Mill Fever* —Almost all workers suffer from *mill fever* or *cotton cold* when they begin to work in the cotton mills and a similar illness occurs on first exposure to the dusts of flax grain and malt Tolerance is established usually within a few days though symptoms may reappear following an absence from work for a time as short as 2 to 4 weeks Mill fever begins within 12 hours of exposure to the dust The temperature may rise as high as 103 F but returns to normal over night Headache malaise and exhaustion accompany the fever and occasionally nose bleeding nausea and vomiting occur Symptoms may reappear each night for the first few days or even weeks of exposure but most workers become acclimatised within the first month

(2) *Byssinosis* —

Synonyms —Strippers Asthma Grinders Asthma Cotton Card Room Asthma

Ætiology —The illness begins suddenly after many years of exposure to dust in the cleaning and carding of cotton especially in men who strip and grind the carding machines

Symptoms —Three stages are recognised in its development In the first stage the worker complains of an irritating cough with tightness in the chest and breathlessness usually on Monday hence the name *Monday fever* and he remains well for the rest of the week. In the second stage the symptoms extend over more days in the week and finally become permanent In the third stage the byssinosis is disabling tightness of the chest and dyspnœa due to chronic bronchitis and emphysema are so distressing that the worker has to leave the cotton industry

Treatment —The condition is reversible only in the early stages and for recovery to take place there must be complete withdrawal from exposure to cotton dust The treatment of chronic bronchitis and emphysema is discussed on p 1000

(3) *Weavers cough* —This is an acute illness confined to workers employed in cotton weaving sheds Outbreaks have always been associated with the handling of mildewed yarn which suggests that the causal agent is a fungus Tightness of the chest retrosternal pain dyspnœa and cough productive of purulent sputum are the

to the passage of electricity it is one of the essential minerals in the electrical industry Radiographs of workers exposed to mica dust have shown diffuse shadows in the *middle zones of the lungs sometimes with fibrosis of the peribronchial type*

(*b*) FULLER S EARTH

Fuller s Earth is an absorbent of grease and is used for the filtration of mineral oils, and as an ingredient of soap, wall papers and toilet requisites Fine punctate mottling with some co alescence has been described in the radiographs of men exposed to the dust The necropsy appearance is that of a soft patchy pneumoconiosis unlike the hard nodular appearance of silicosis

(*c*) KAOLIN

Kaolin or china clay is used in the manufacture of paper in ceramics as a filler in the rubber industry for paints for wall plasters and white Portland cement Extremely fine mottling or reticulation has been described in the radiographs of a *number of workers exposed to the dust*

5 NON PATHOGENIC INORGANIC DUSTS

The dusts of the salts of calcium, iron tin and barium are inert when inhaled and give rise to the *benign pneumoconioses* (see p 1009) Particles small enough to *enter the alveoli are engulfed in phagocytes which are either coughed up or deposited* in the aggregations of lymphoid tissue at the bifurcations of the bronchioles Radio graphic shadows may be produced the density of which varies directly with the *atomic weight of the element in the compound concerned Calcium (atomic weight* 40) inhaled as the dust of limestone marble lime or cement may give rise to non progressive arborescent shadows Iron (atomic weight 56) can cause reticulation or nodulation The radiographic appearances in the chest of an electric arc welder may be identical with those of silicosis but *welders siderosis* can be distinguished from silicosis by the complete absence of disability *Stannosis* a condition which results from the inhalation of salts of tin (atomic weight 118) gives rise to scattered dense punctate shadows with no associated symptoms or abnormal physical signs In *baritosis* or barium pneumoconiosis (atomic weight 137) there is no disability, but in radiographs there are small sharply circumscribed nodules evenly distributed throughout the lung fields

6 *PATHOGENIC INORGANIC DUSTS*

Aluminium is capable of producing fibrotic pulmonary lesions and manganese cadmium and vanadium give rise to chemical pneumonitis Both types of reaction can follow the inhalation of beryllium and its compounds (see p 385)

(*a*) ALUMINOSIS

Exposure to the inhalation of aluminium dust in Germany during the War of 1939–1945 gave rise to a condition known as *aluminosis* or *aluminium lung* The development of the illness was rapid and appeared to bear no relation to the length of exposure to the dust A dry cough with pain on breathing shortness of breath anorexia and gnawing abdominal pain were the main symptoms Radiographs showed focal shadows in the apices with a reticular appearance in the upper and middle zones later becoming confluent Spontaneous pneumothorax occurred in a few of the cases

8 ANIMAL DUSTS

The dusts of leather silk wool fur hair, bone horn and ivory are of minor importance in the causation of respiratory disease On the other hand the danders of cat, dog and horse, and the feathers of birds may be responsible for asthma Animal dusts sometimes carry infections especially anthrax (see p 79)

DONALD HUNTER

PULMONARY TUBERCULOSIS

Synonyms —Phthisis Consumption

Pulmonary tuberculosis embraces all the abnormal conditions induced by infection *of the lungs pleuræ and bronchial glands with the tubercle bacillus*

Ætiology —Predisposing Causes —*Age* —The maximum age incidence is between the fifteenth and forty fifth years although the disease may be encountered at any age Senile tuberculosis is more common than is generally recognised

Sex —The disease is more frequent in males but between the ages of 5 and 15 the female sex shows a preponderance

Heredity —Pulmonary tuberculosis certainly occurs with undue frequency in certain families Since the direct transmission of the tubercle bacillus to the infant is extremely rare two explanations seem possible—(1) Children born of tuberculous stock may inherit an increased susceptibility or diminished resistance the tuberculous diathesis or (2) they may contract tuberculosis on account of their exposure to massive infection in early life

Race —Native races suffer severely when first exposed In Europe people from isolated rural areas who migrate to cities are particularly susceptible with a high mortality and a high morbidity long urbanised races like the Jews are said to be relatively resistant

Occupation —The highest mortality from tuberculosis occurs in England amongst the workers in dusty occupations and conditions leading to overwork or to under feeding increase the liability to the disease

Environment —Overcrowding defective sanitation dampness dirt lack of sun light and insufficient ventilation are most potent factors in the spread of the disease causing both lowering of the resistance and increased facilities for direct infection

Trauma —Trauma involving the chest wall may be followed by active pulmonary tuberculosis *This is probably because the injury leads to activity of previously* arrested disease rather than to fresh infection at a spot of lowered resistance

Psychological —Psychical factors such as sudden mental shock grief or dis appointment may influence the outcome

The influence of other diseases and conditions —The following diseases predispose to the development of pulmonary tuberculosis measles especially when complicated by broncho pneumonia whooping cough influenza pneumoconiosis alcoholism diabetes syphilis congenital heart disease and insanity Tuberculosis may manifest itself for the first time during prolonged lactation or after repeated pregnancies when previously existent it often remains quiescent during pregnancy but it may spread rapidly after childbirth Contrary to the usual belief pulmonary tuberculosis not infrequently coexists with mitral stenosis Cases apparently following pneumonia *pleurisy or bronchitis are usually tuberculous from the onset*

EXCITING CAUSES —The causal organism is the *Mycobacterium tuberculosis* dis covered by Koch in 1882 It exists in four main forms human bovine avian and reptilian only the two former usually occur in man but avian infection has been recorded The human type is found in over 97 per cent of pulmonary tuberculous lesions though a higher proportion of the bovine type has been found in Scotland In glandular tuberculosis up to the age of 5 years over 80 per cent of the bacilli

main symptoms malaise, fever, frontal headache and aching pains in the limbs and back may also be present

(4) *Acute respiratory illness from contaminated cotton*—Contamination of cotton with *Aerobacter cloacæ* has been responsible for epidemics of an acute febrile condition in workers exposed to its dust Symptoms begin within the first 6 hours of exposure and include anorexia headache, vomiting cramp like abdominal pain and sometimes rigors The illness usually persists for 2 to 5 days

(*b*) FARMERS' LUNG

This condition follows the inhalation of the dust of mouldy hay or grain and fungus infection is probably a factor in its ætiology although its exact role has not been determined Cowmen and members of mobile threshing teams are especially at risk The clinical picture is that of chronic bronchitis and emphysema, which becomes progressively more severe with continued exposure Radiographs in the early stages show a fine alveolar mottling with evidence of compensatory emphysema In the later stages there is an increase in the density of the mottling and patches of opacity due to coalescent areas of fibrosis appear, with increase in the hilar and peri hilar shadows The patient must be removed from dusty work and treated with potassium iodide The prognosis is good

(*c*) BAGASSOSIS

Bagasse is the cellulose fibre of sugar cane which remains after the sugar has been extracted It is used for making boarding for the interior decoration of buildings and for thermal insulation Exposure to the dust occurs when workers use a shredding machine to break up the bales of bagasse The dust may give rise to a self limited respiratory infection with acute bronchiolitis severe dyspnœa, cough productive of scanty sputum and sometimes hæmoptysis Radiographs show miliary shadows throughout the lung fields There is usually gradual improvement with recovery in 6 weeks Rarely impaired resolution occurs and may lead to pulmonary fibrosis with the radiographic appearance of thick bands of fibrous tissue traversing the lung fields and simulating cavities

(*d*) PAPRIKA

In Hungary and Yugoslavia along the Danube the fruits of the paprika plant when picked late in the season are often infected with the mould *Mucor stolonifer* The dried fruits are made into red pepper and inhalation of the spores and mycelia by the paprika splitters may give rise to acute bronchitis and later to fibrosis of the lungs and bronchiectasis The grinders and packers of the red pepper never suffer in this way

(*e*) WOOD

Bronchial asthma can be due to allergy to wood dusts in particular to those of the South African boxwood (*Gonioma kamassi*) mansonia wood (*Sterculiacea altissima*) and Western red cedar (*Thuja plicata*) Gum acacia is the allergen responsible for *printers asthma* which occurs in men exposed to a spray used in colour printing to offset one printed page from the next It can be eradicated by the substitution of dextrose for gum acacia in the spray fluid

results in the formation of a structureless cheesy mass Further changes may now occur either softening with the development of a cold abscess filled with tuberculous pus' or calcification with the subsequent formation of gritty masses known as pneumoliths

2 *Cavitation* —Cavities result from the liquefaction of caseous areas and the expectoration of the resulting debris They may be no larger than a pea or may occupy the whole of one or more lobes A recent cavity has an irregular outline with rough shaggy walls and a vascular line of demarcation It is often traversed by trabeculæ formed by bronchi and vessels which may be partly or completely obliterated, while sometimes the trabeculæ consist of condensed lung tissue which originally separated adjacent cavities In chronic cases the cavity is surrounded by fibrosed lung tissue forming a pseudo capsule and its interior becomes lined by a thin smooth false membrane Small aneurysms may be found arising either from vessels running in the walls or in the trabeculæ of the cavity the former being the more common In some cases where hæmoptysis has occurred rupture of such an aneurysm is the cause

3 *Fibrosis* —Reactive changes in the lung stroma lead to the formation of fibrous tissue This may occur early or after caseation has taken place

In the majority of deaths from all causes old tuberculous lesions are found post mortem near the apex of one lung These consist of small nodules of arrested disease with thickening and dimpling of the adjacent pleura

Dissemination in the Lungs —The disease may spread from the primary peribronchial deposit—(*a*) by direct infiltration (*b*) by the peri bronchial lymphatics and capillaries leading to a racemose appearance or to peri bronchial fibrosis (*c*) by the subpleural and interstitial lymphatics with localised miliary dissemination (*d*) by inhalation into a bronchus of tuberculous material which is then carried to other parts of the same or to the opposite lung—this not infrequently happens after hæmoptysis and in cavitation (*e*) by the blood vessels *e g* generalised miliary tuberculosis may result from erosion of a caseous tubercle into a vein

The pathology of the clinically distinguishable forms of pulmonary tuberculosis will now be described

1 Acute Miliary Tuberculosis —A primary caseous focus may be discovered at the apex of one lung in the bronchial glands or at some distant spot in the body Local erosion of a vein may be found accounting for the dissemination of the disease The lungs are usually studded with minute grey tubercles the smaller ones requiring a hand lens for their recognition In very acute cases death occurs before any secondary broncho pneumonic changes take place Miliary tuberculosis may develop as a terminal event in chronic fibro caseous or fibroid tuberculosis The tubercles are then found in large numbers around the old foci of disease but to a less extent in the more remote portions of the lung

2 Chronic Miliary Tuberculosis —Reports of cases of this condition were commoner before the recognition of sarcoidosis and many cases were probably erroneously diagnosed It is questionable whether real chronic miliary tuberculosis exists although even before the use of streptomycin there were great divergences in the rapidity of development of miliary cases and some might almost have been termed subacute although their fatal termination was the same

3 Acute Caseous Tuberculosis —Large areas of consolidation form rapidly, which differ histologically from the common chronic tuberculous broncho pneumonia in that the alveolar exudate is more definitely inflammatory and contains fibrin In the rare lobar cases the rapid caseation and the presence of tubercle bacilli show that the caseous pneumonia is a specific process Firm yellowish patches which may be confluent are seen usually scattered throughout both lungs The affected areas are airless and sink in water Softening is generally present in varying forms up to actual cavity formation which may be extensive involving even a whole lobe

isolated conform to the bovine variety In tuberculosis of bones and joints up to the same age 29 per cent of the cases are of bovine origin

The bacilli may gain access to the body by inhalation by alimentary ingestion through the tonsils through the skin or possibly, in rare instances by hereditary transmission It is probable that in the majority of cases of pulmonary tuberculosis in adults, the organisms are carried direct to the lungs in the inspired air, and Ghon showed that in children who had died of tuberculosis of the lungs, a primary focus was present in the lungs in 92 4 per cent Calmette and others have demonstrated that the bacilli may gain access to the bronchial glands from the alimentary tract through the thoracic duct, or from the tonsils through the cervical and mediastinal glands but this is now considered to be an exceptional path of infection Cases have been recorded in which primary cutaneous infections have been followed later by active pulmonary tuberculosis Direct intra uterine transmission of the tubercle bacillus if it occurs at all must be so rare that it is a factor of negligible importance

The incubation period of tuberculosis is uncertain owing to the difficulty of deter mining when infection takes place It is believed by many authorities that the majority of individuals in a semi rural or semi urban country like Great Britain are originally infected in infancy early childhood or youth by the inhalation of bacilli in infected spray droplets or dried dust, or else by ingestion of bovine or occasionally human bacilli The inhaled bacilli produce a lesion in the tissue known as a primary lesion which has special characteristics

The focal lesion is relatively slight but the reaction in the regional glands is much more obvious and characteristic Three possible things may happen as a result of the tuberculous lesion The lesion may disappear leaving little or no trace the focal lesion and the regional glands may become fibrous and then calcified as described by Ghon, or the focal lesion or the glands may break down and infection may spread locally or generally through the blood stream

What happens in an individual infection depends on the dose of infection the age and general condition of the infected person and possibly the degree of inherited resistance to tuberculous infection The earlier the age at which infection takes place, the more serious the result

Following infection acquired resistance develops to a greater or lesser extent and is probably permanent The acquired resistance modifies the effect of any subsequent infection so that in post primary tuberculosis there is a much more severe focal reaction than in the primary infection and little or no regional glandular reaction It has been held that reinfection does not take place but that all tuberculosis subsequent to the primary infection is a reactivation or a spread from the original focus just as tertiary gummata in syphilis are not evidence of reinfection but of spread from an original primary chancre This theory would tend to discount the danger of contact infection in later life but, in fact there is a great deal of evidence to show that re infection is the common cause of post primary tuberculosis

Pathology—The earliest lesion in the lung is the formation of tubercles whose structure is described in the general article on tuberculosis Whereas pulmonary primary lesions may appear anywhere in the lung post primary lesions for some reason not understood generally appear first at one or other apex Each lesion often appears radiologically as an area of localised opacity in the subclavicular area This lesion was described first of all by Assmann although the lesion he described was from 1 to 2 in in diameter and probably consists of a tuberculous lobular collapse When the lesions are small they are described as minimal lesions Both these lesions may and often do develop into progressive tuberculous infiltration

SECONDARY CHANGES—1 *Caseation*—The tubercle is avascular and owing to this and possibly also to the action of tubercle toxins coagulation necrosis and fatty degeneration frequently ensue This combined process is known as caseation and

(e) *Laryngeal*—Hoarseness or aphonia may be the first symptom but laryngeal tuberculosis is almost invariably secondary to pulmonary disease although the latter may have been unsuspected

(f) *Gastro intestinal*—Anorexia and flatulence often occur early When they are accompanied by slight loss of weight and pyrexia the possibility of pulmonary tuberculosis should be suspected

(g) *Pleural*—Dry pleurisy is a frequent manifestation of latent pulmonary tuberculosis When a serous effusion develops its tuberculous character can be determined by laboratory investigations Pneumothorax developing in a previously healthy individual is a rare but often serious clinical mode of onset

(h) *Pneumonic*— Galloping consumption often begins with pneumonic manifestations especially in the young

(i) *Associated with other diseases*—Tuberculosis may follow immediately on an attack of measles, influenza or whooping cough especially if complicated by broncho pneumonia In some cases it develops at a later period after the acute disease

(j) *Senile*—In old people an insidious onset is common The disease may be of bronchitic type and the signs are often masked by emphysema There may be little or no rise of temperature Sometimes pneumonic or broncho pneumonic tuberculosis of the type more familiar in infants is found Sometimes the differential diagnosis is from bronchial neoplasm

THE CHIEF SYMPTOMS of pulmonary tuberculosis are—

Cough—This varies considerably in different types of disease It may be very slight or absent in generalised miliary tuberculosis or in any form in the insane It is sometimes dry persistent and ineffective especially in miliary extension in the lungs from an old focus of disease in bronchial gland tuberculosis or in pleurisy When there is associated bronchitis or caseation the cough is usually accompanied by expectoration which if very tenacious may lead to retching or even to vomiting particularly in the morning In laryngeal tuberculosis the cough is husky and frequently painful

Expectoration—In early disease there is usually no sputum and in some cases more especially in the fibroid type widespread lesions may be present with practically no expectoration When caseation is in progress or when there is secondary infection with bronchitis the sputum may be abundant and amount to as much as 20 or more ounces in the 24 hours It may be clear or mucoid or thick tenacious muco pus If mucoid it often contains small particles the size of a pin s head or larger of yellow caseous material Nummular sputum may be met with in active caseous disease especially with excavation This consists of flat rounded masses of muco pus with a somewhat distant resemblance to coins In tuberculosis the sputum is usually inoffensive If bronchiectasis or gangrene occurs as a complication the expectoration becomes typically malodorous Pulmonary calculi or pneumoliths composed chiefly of calcium carbonate or phosphate are sometimes expectorated They vary in size from a pin s head to a pea are irregular in outline and sometimes branched being derived generally from the walls of a cavity Although the occurrence of these does not necessarily indicate fresh activity in the lungs yet such a possibility should always be suspected and a careful watch maintained on the temperature during the next few days In some cases larger pneumoliths as big as a cherry may be coughed up, and those are frequently derived from calcified tracheo bronchial glands They may give rise to alarming symptoms at once and be the forerunner of fresh activity in the lungs

Microscopical examination—The presence of tubercle bacilli in the sputum is the most decisive test of the existence of this disease The small yellowish caseous particles should be selected from the sputum and appropriately stained If no tubercle bacilli are found samples from the whole sputum of the 24 hours concentrated by the antiformin method can be examined Droplets collected on a laryngeal

4 FIBRO CASEOUS TUBERCULOSIS —This is the commonest variety of the disease the appearances of the lung vary with the relative preponderance of the caseous and fibrotic changes The early lesions are miliary or broncho pneumonic but areas of caseation in varying stages including cavitation, are almost always present The older lesions show considerable fibrosis the strands of sclerotic tissue being pigmented and glistening The earliest lesion is usually near the apex of the upper lobe at the back *more rarely a little lower and towards the front* From this focus disease may spread directly or through the lymphatic bronchial or the vascular system to adjacent or distant parts of the lung An open cavity from which infected sputum can overflow and pass or be aspirated through the bronchial tree to lower parts of either lung is to be regarded as particularly dangerous Pleural adhesions are usually present over the oldest lesions and in the interlobar fissures

5 FIBROID TUBERCULOSIS —Fibrosis may be localised around a small arrested lesion, or may spread throughout a lung in which caseation or excavation has occurred One lobe or the whole lung is then contracted and firm In the interstices of the fibrous tissue which is usually pigmented inspissated caseous material calcareous patches or cavities are seen The shrinkage may lead to bronchiectasis especially in the lower lobes The overlying pleura is much thickened and adherent and the mediastinum is drawn over towards the affected side The opposite lung or the sound portions of the fibrosed one, may show compensatory emphysema

The bronchial glands —The tracheo bronchial glands are affected in all forms of pulmonary tuberculosis In post primary disease the glandular lesions are insignificant as a rule whereas in primary disease, depending on the stage of the disease they show considerable enlargement caseation or fibrosis with deep pigmentation and calcification Occasionally in apical tuberculosis the cervical glands on the affected side are involved

The pleura —This too is almost constantly affected The commonest changes are an early dry pleurisy and a later thickening with adhesions which may completely unite the visceral with the parietal layers In acute disease or active spread the pleura may be studded with miliary tubercles leading to a large serous effusion

The post mortem appearances of the lesions situated in the other organs found as complications of pulmonary tuberculosis are described in the respective sections dealing with them and include tuberculous meningitis peritonitis enteritis genito urinary tuberculosis and osseous tuberculosis There is usually atrophy of the skeletal muscles sometimes lardaceous and fatty degeneration of the liver and hypoplasia with fatty degeneration of the heart

Symptoms —The symptoms fall into three groups (Pottenger)—(1) pulmonary such as catarrh expectoration hæmoptysis and pleurisy (2) reflex such as pain cough and laryngeal irritability (3) toxæmic including malaise tachycardia pyrexia and loss of weight

ONSET —The mode of onset is very variable but certain forms can be recognised

(*a*) *The diagnosis is made by a routine radiological examination* and the patient has no symptoms whatever This does not unfortunately mean that the lesion can be ignored it may be the golden moment for treatment

(*b*) *Insidious* —The early symptoms may be malaise anæmia amenorrhœa cardiac irritability progressive loss of weight and slight rise of temperature *generally towards* evening Cough and expectoration often appear only when the signs in the chest are quite apparent

(*c*) *Catarrhal* —Colds which appear to persist with fatigue and persistent cough should be regarded with suspicion

(*d*) *Hæmoptysis* —Hæmoptysis may first draw attention to the lungs It may be slight and is then due to early inflammation around the focus of infection If it is more marked it may afford dramatic *evidence of extensive* disease which had not been recognised previously or arise from an old unsuspected cavity

(*a*) In acute miliary tuberculosis it may be continuous or remittent and the typus inversus is not uncommon the morning temperature being higher than the evening This is generally regarded as a sign of grave prognosis

(*b*) In acute caseous tuberculosis the high temperature at the onset is continuous and the record resembles a pneumonic chart When caseation occurs it becomes hectic or intermittent with a daily swing of 4° or 5° F This is probably due to the action of tubercle toxins and not to the presence of a secondary infection

(*c*) In chronic fibro caseous tuberculosis there is no characteristic temperature record There may be only a very slight rise occurring at intervals of a few days On the other hand the patient may be afebrile while resting but febrile when ambulant Further an afebrile ambulant patient may over exert himself and develop a sharp rise of temperature which subsides in a few days with rest The temperature chart is thus a guide to prognosis and to treatment and if acute miliary tuberculosis or caseation occurs a typical temperature variation ensues

(*d*) In fibroid tuberculosis the temperature is usually normal unless excessive auto inoculation results from exercise or the disease advances The occurrence of hæmoptysis may have a very definite effect upon the temperature In some cases it is not followed by pyrexia but if the inhaled blood leads to a hæmoptoic bronchitis there may be a slight degree of fever lasting for a few days When a definite and persistent pyrexia follows it usually indicates activity around an old focus of disease, or fresh spread by inhalation of blood containing tubercle bacilli to distant parts of the lung

A premenstrual rise of temperature may occur but as it is also met with in healthy women it is not pathognomonic.

Hæmoptysis—Hæmoptysis occurs at some stage of pulmonary tuberculosis in about 50 per cent of all cases With early lesions the sputum is only streaked This may result from the inflammation of tuberculous bronchitis or from a small area of collapse or broncho pneumonia Profuse hæmoptysis generally occurs in chronic disease but it is occasionally met with in acute caseous forms Recovery may take place after coughing up 2 or 3 pints or death may ensue rapidly from suffocation before any considerable quantity of blood has been expectorated After the cessation of bleeding the sputum may be blood stained for several days the colour becoming darker The source of profuse hæmoptysis is generally an aneurysm of a branch of the pulmonary artery lying in a cavity or in a fibroid lung although occasionally ulceration without previous aneurysm formation may occur In the majority of cases hæmoptysis begins while the patient is lying down or resting so that exercise or work are not frequent exciting causes

The patient notices a salt taste feels a warm gush in the mouth and then expectorates the blood He is usually greatly alarmed flushed and sweating with rapidly beating heart The blood at first is as a rule bright and frothy but some clots may be present later it is mixed with muco purulent expectoration in the form of clots or streaks

Circulatory system—The heart may be small but the right side often hypertrophies in chronic fibroid cases Tachycardia may be due to nervousness but when constant it generally indicates active disease or over exertion on the part of the patient The blood pressure is usually low in the stages of activity and a steady rise during treatment is a favourable sign

The blood—The red cells are usually normal in number but there may be a slight anæmia On the other hand when there is much cyanosis or after sanatorium treatment the red cells may be increased In the early stages the leucocytes may be slightly increased A polymorphonuclear leucocytosis occurs in caseation and in early cavity formation and at times with secondary infection of the lungs In pyrexial cases the sedimentation rate is raised as a rule Although the rate is raised in active disease a normal level cannot unfortunately be regarded as evidence of arrested

mirror by cough induced by it may be examined for the presence of tubercle bacilli, especially in children or in patients who habitually swallow sputum In similar cases, tubercle bacilli may be found by gastric lavage

Sputum culture by the Loewenstein or Dubos method may be of value when tubercle bacilli are not found in smears The cells present are usually of the mono nuclear type either mononuclear leucocytes or altered alveolar epithelial cells The presence of elastic tissue indicates that destructive pulmonary lesions are in progress Secondary infecting organisms may be demonstrated by cultural methods Failure to find tubercle bacilli in the sputum does not in any way exclude pulmonary tuber culosis since their detection depends on chance and diligence as well as on the stage of the disease Persistently negative sputum in patients with large quantities of purulent sputum should, however, suggest the possibility of alternative infections

Dyspnœa —Slight dyspnœa occurring early in the disease may be due to dimin ished movement of the diaphragm on the affected side In more advanced cases the degree of dyspnœa is proportional to the amount of lung tissue involved In addition, cough and pyrexia play a part in its production Complications such as pleurisy pleural effusion pneumothorax and cardiac failure increase the shortness of breath It is rare to find orthopnœa even in acute and rapidly spreading disease In arrested cases the dyspnœa is proportional to the extent of fibrosis

Cyanosis —This is not an early symptom of tuberculosis It is dependent upon the amount of lung tissue involved but is increased by the coexistence of emphysema or cardiac failure The ' hectic flush ' of tuberculosis is a vasomotor effect caused by toxæmia

Pain —Not every sufferer from tuberculosis experiences pain even in the acute stages of the disease The commonest cause of pain is dry pleurisy When the diaphragmatic layer of the pleura is affected, pain may be referred to the epigastrium or to the corresponding shoulder In chronic fibroid phthisis there is frequently a dull, aching pain in the chest It may be caused by the contraction of the condensing fibrous tissue Cutaneous tenderness of the chest wall is met with in some cases of advanced disease, and is probably due to a cachectic neuritis A cold abscess forming along one of the ribs or costal cartilages is a rare cause of localised pain in the chest-wall Cough may be painful especially when paroxysmal or frequent the pain being referred to the costal attachments of the diaphragm and upper abdominal muscles The sudden occurrence of pneumothorax may cause such severe pain as to induce collapse, but when of more gradual onset no severe discomfort may be experienced Tuberculous laryngitis may be the cause of very great suffering

Night sweats —Although not pathognomonic night sweats occur more frequently in tuberculosis than in other diseases They are met with in all stages of active lesions, and may be of great severity

Loss of weight —This is often an early symptom It is most marked in acute disease and in the late stages of chronic fibro caseous tuberculosis

Fever —Pyrexia is one of the most important indications of activity at any stage of pulmonary tuberculosis although it does not follow that the disease is arrested when there is no fever During treatment the temperature should be recorded at certain definite hours in the day (*a*) On waking The normal mouth temperature at 7 or 8 a m is 97° or 98 F in the mouth and 97 2° to 99° F in the rectum This temperature should be taken in bed before eating or drinking (*b*) At 1 p m , after the hour s recumbent rest (*c*) At 6 p m (*d*) At 9 p m after retiring to bed The maximum temperature is usually reached between 4 and 6 p m but may be delayed to 8 or 9 p m The temperature is dependent upon the extent and the activity of the disease and upon the amount of exercise taken Only 5 minute readings should be accepted

Adventitious sounds may be absent but usually fine or medium crackling râles are heard with inspiration especially after coughing When active softening is in progress the râles frequently become coarse and crackling The voice conduction is much increased bronchophony and whispering pectoriloquy being audible

THE PHYSICAL SIGNS OF EXCAVATION —Flattening of the chest wall and diminished movement over the cavity are now more marked if the cavity is apical there is in addition notable dropping of the shoulder and wasting of the shoulder girdle muscles

The diminution of movement is confirmed by palpation Vocal fremitus is generally increased owing to the surrounding consolidation but if the cavity is full or there is much pleural thickening it is diminished

The percussion note is dull when the cavity is small or filled with secretion A peculiar boxy or cracked pot' note the bruit de pot fele is obtained over large superficial cavities especially when communicating with an open bronchus This is best heard on percussing with the mouth open and Wintrich showed that the note may be altered in pitch over such cavities when percussing with the mouth open or closed apart from the actual presence of the cracked pot sound

The breath sounds are bronchial broncho cavernous cavernous or amphoric, according to the size of the cavity and to the amount of its contents When it is full the breath sounds may be distant weak or even absent and this is especially noticeable in basal bronchiectasis

With a dry cavity there may be no adventitious sounds Usually râles are audible they may be medium or large and bubbling or crackling in character Over a large cavity a metallic tinkle and amphoric echo may be heard With a very large cavity extending through the whole of one lung a typical *bruit d airain* is at times obtainable Voice conduction is increased bronchophony and whispering pectoriloquy are present and in some instances post tussive suction is heard Some cavities are only revealed by radiographic examination or by tomography

THE PHYSICAL SIGNS OF FIBROSIS —The chest is asymmetrical the affected side being flattened and moving little while compensatory scoliosis or kypho scoliosis is often present The cardiac impulse is seen to be displaced towards the affected lung and may be higher or lower than normal It may be drawn over to the right axilla or on the left side as far back as to the posterior axillary line or even to the angle of the scapula The intercostal spaces may be retracted and dilated venules are sometimes seen over the front of the chest as the result of obstruction caused by displacement of the mediastinum and traction on the deeper veins

Diminution of movement is confirmed by palpation and the cardiac impulse can be more accurately localised Vocal fremitus may be increased or diminished the former occurs when the lung is consolidated and the large bronchi patent the latter when there is much pleural thickening

The percussion note over fibroid lung is dull and the sense of resistance increased unless cavities are present The opposite lung may be hyper resonant and its resonance extend across the mid sternal line The cardiac dullness is often continuous with that of the fibroid lung and its area can only be determined by the cardiac pulsation

The breath sounds may be weak and distant or bronchial in character depending on the patency of the bronchi and the presence of cavities

Often there are no adventitious sounds although fine or medium rales of a sticky or metallic nature may be heard The voice conduction may be diminished or there is pectoriloquy and bronchophony

It must be borne in mind that in actual disease the lesions are not so clear cut and well defined In a case of some duration different stages of disease can be found in the same individual thus infiltration consolidation with softening excavation and fibrosis may be present in different lobes of the lungs and thus it may be possible to determine the site of origin and path of spread of the disease

disease as the initial rate is not infrequently normal in spite of progressive disease

Alimentary system —The tongue is usually clean and the appetite good even in cases with marked fever When tuberculosis of the larynx is present there is frequently severe dysphagia Dyspepsia may be complained of, anorexia flatulence and distension with nausea are the commonest symptoms pain being rarely noticed There may be marked intolerance of fat in the diet Atonic dilatation of the stomach may occur in some cases towards the end of the disease

Nervous system —The classical spes phthisica is rare, but when present is very striking by its contrast with the realities of the disease It should be remembered that the reality of the disease is known only to the physician and not the patient and it might be as reasonable to talk about spes carcinogenica' in a patient who has no idea that he has a growth Spes phthisica is sometimes a bold front put up by a patient and stands in sharp contrast with the depression and melancholia which often affects patients whose lesions are slipping Patients with chronic tuberculosis sometimes become emotional and self centred but most of the psychological changes are the result of the long periods of treatment and frequent disappointments characteristic of the disease and are not caused by the disease itself Insomnia may be due to cough pyrexia night sweats or pain, especially laryngitis With marked cachexia a definite peripheral neuritis may occur

Genito urinary system —In the early stages there is often an increased sexual desire and this may recur when arrest is taking place This is probably in part due to the therapeutic regime, the rest abundant food and lack of interesting occupation reacting upon the nervous system of young adults In advanced disease all sexual desire is lost Menstruation ceases early and occasionally the patient may seek advice for amenorrhœa but this occurs more often in acute or advanced cases Women remain fertile even in advanced disease The urine is normal in the early stages, later a febrile albuminuria may occur or in advanced cases an amyloid nephrosis with generalised œdema may develop

THE PHYSICAL SIGNS OF EARLY DISEASE —*There are no physical signs in really* early disease and the diagnosis is a radiological one At a later stage diminished expansion of an apex may be found together with slight impairment of percussion note and slight increase of breath sounds and voice conduction An important physical sign is the presence of fine post tussive crepitations at one or both apices *Many of the physical signs described in previous days as signs of early tuberculosis* although they can be found by the skilled examiner are now really only of historical interest and none replace a radiological picture in accurate diagnosis

PHYSICAL SIGNS OF ACUTE MILIARY TUBERCULOSIS —If the condition develops acutely from breaking down of an infected bronchial gland or small lung focus the physical signs are generally those of an acute generalised broncho pneumonia unless there is meningeal involvement as well in which case the pulmonary symptoms and signs are masked or obscured by those of the cerebral involvement When miliary tuberculosis occurs as a terminal event in a chronic case marked dyspnœa cyanosis and tachycardia are early symptoms There may be crepitations or fine crepitant râles widely distributed over both lungs and sometimes areas of tubular breath sounds especially in the lower lobes The original signs are often masked or less apparent This is especially the case if meningeal involvement occurs also

THE PHYSICAL SIGNS OF CONSOLIDATION —Limitation of movement and flattening over the affected part of the lung usually the apex is now more noticeable

The diminution of movement is confirmed on palpation and vocal fremitus is found to be *definitely increased*

The pulmonary resonance is diminished to definite dullness and the sense of resistance is correspondingly increased

The breath-sounds are bronchial

Fatty degeneration of the myocardium occurs as a result of toxæmia and infection by direct spread along the lymphatics may lead to pericarditis The peripheral circulation is not infrequently poor, chilblains are common and cachectic purpura may be seen Lardaceous degeneration as a consequence of chronic tuberculosis is not so common nowadays as formerly but when present may affect the liver spleen intestines lymph glands and kidneys

The genito urinary complications include lesions in the kidneys bladder epididymis and prostate If the suprarenal body is affected Addison's disease will usually develop Spinal caries is occasionally observed A peripheral neuritis may form part of the lesions occurring with marked cachexia Generalised dissemination of the tubercle bacilli by the blood-stream is followed by tuberculous meningitis

Diagnosis —This is easy when definite signs are present in the lungs and when tubercle bacilli are found in the sputum On the other hand the diagnosis of early cases may present one of the most difficult problems in clinical medicine Tuberculosis may be suspected on account of symptoms although the physical signs are indefinite The conditions which most frequently lead to doubt are dyspepsia neurasthenia debility tachycardia associated with early Graves disease or heart disorders affections of the nose and throat and in children enlargement of the bronchial glands The history and symptoms are of great importance in these cases and a careful examination should be made of each system A test meal opaque meal or blood examination may be required before the correct diagnosis is established

On the other hand there may be definite signs of disease in the lungs which have to be differentiated from those produced by other conditions simulating tuberculosis The cases included in this group embrace the majority of pulmonary lesions especially chronic bronchitis fibrosis bronchiectasis asthma, emphysema apical collapse pleurisy new growths and cysts Diagnosis depends upon the history and course of the disease together with a careful record of the physical signs in the chest, investigation of the sputum for infecting organisms radiographic examination and in some cases the determination of the Wassermann reaction

A condition of special difficulty is that of the variety of sarcoidosis known as Boeck s sarcoid The lesion is a benign lymphogranuloma or reticulosis It affects the lymph glands lungs bones especially those of the fingers and the skin (see pp 1045 1245) The parotid and lachrymal glands are sometimes involved and iridocyclitis has been recorded in 10 per cent of the cases The intestines spleen and liver may be affected The chief diagnostic points are the character of the skin lesions and the chronicity and tendency to spontaneous arrest Tubercle bacilli are not found and the Mantoux reaction is often negative The radiological appearances in the lungs are those of a diffuse mottling—coarser than that of miliary tuberculosis The hilar glands are often markedly enlarged

When the diagnosis still remains doubtful the patient should be placed under observation and a series of examinations carried out the object of which is to determine whether or not active tuberculosis is present The temperature should be observed with the patient in bed a daily rise to 99 F or a swing of 1 5 to 2 below normal being suspicious The sputum should be examined repeatedly for tubercle bacilli by the ordinary method and if not found the antiformin process should be carried out and gastric washings should be examined and cultivated

The sedimentation rate of the erythrocytes is affected in this disease In active cases the sedimentation rate is increased but this reaction is not specific It is also increased in other conditions such as pregnancy carcinoma syphilis rheumatism and acute infections The test is therefore of little or no value in diagnosis but it affords valuable indications of the degree of activity and may assist in determining the form of treatment A normal sedimentation rate unfortunately does not necessarily mean that the tuberculous disease is quiescent As in radiology it is often the serial records that are most valuable

Certain other signs are occasionally seen in pulmonary tuberculosis

Myoidema is an undue irritability of the muscles to direct mechanical stimulation revealing itself by a flickering fibrillary contraction on tapping with the finger, and may occur in tuberculosis at all stages It is best seen over the pectoralis major on the affected side It may be present quite early, but is not pathognomonic, as it may occur in any cachectic state

Clubbing of the fingers is commonly seen in chronic cases, the nails are curved and present a parrot beak appearance, the thumb index and middle fingers being most affected Drum stick clubbing is only seen in fibroid lesions with bronchiectasis

EPITUBERCULOSIS —This term was applied by Eliasberg and Neuland in 1920 to a condition of consolidation in tuberculous infants, often affecting a whole lobe In spite of definite physical signs and characteristic radiological appearances there are few symptoms and recovery is the rule with fairly rapid clearing of the radiographic shadows from the periphery inwards It is probably due to atelectasis of a lobe in whole or part due to bronchial obstruction from enlarged hilar glands

PULMONARY OSTEO ARTHROPATHY —In cases with bronchiectasis the joints may be affected, swelling occurring especially in the wrists, ankles and knees and rarely in the hips and shoulders A serous effusion into the joints may be present Pain is usually slight but there is much deformity and functional impairment Radiographic examination reveals productive periosteal changes which may also affect the long bones and the spine (see p 1171)

RADIOGRAPHY OF THE CHEST —Careful study of serial radiographs is essential for the control of the treatment and progress of pulmonary tuberculosis Examination of the chest with the fluorescent screen gives valuable information as to the movements of the diaphragm the cardiac pulsation and the lighting up of the apex of the lungs with inspiration Tomograms often show unsuspected cavities in the lung and are also valuable to show the extent of pulmonary infiltration Close studies of serial pictures are necessary to determine the activity or otherwise of the radiological lesions Opinions as to the activity of lesions on the basis of hardness or softness of the shadows are of little or no value

Complications and Sequelæ —Compensatory emphysema is common in chronic fibroid disease but bronchiectasis occurs less frequently Gangrene of the lung is not often observed Colds and catarrhal affections of the respiratory passages are frequent in sufferers from tuberculosis, and lobar pneumonia may develop as a complication Bronchitis often occurs due either to spread of the tuberculous process or to a secondary infection In some instances asthma appears for the first time after tuberculosis has become manifest A tuberculous abscess occasionally forms about a rib or costal cartilage

Small areas of dry pleurisy are present at some stage in nearly every case a serous pleural effusion is common and an empyema may develop as the result of a mixed infection, or from the tubercle bacillus alone Pneumothorax may occur as an early complication or late in the disease generally from rupture of a caseous focus just under the pleura, this frequently progresses to the formation of a pyo pneumothorax The implantation of tubercle bacilli from the expired air or sputum may lead to secondary foci in the larynx, trachea and epiglottis, or more rarely in the pharynx, tonsils base of the tongue or nose Swallowing of sputum containing tubercle bacilli may give rise to gastro intestinal complications in some cases The most common site of tuberculous ulcers is the terminal portion of the small intestine but the appendix may be affected and the connective tissue around the cæcum is sometimes matted and thickened to form a palpable mass (hypertrophic tuberculoma) Tuberculous peritonitis is not common in adults and is usually secondary to intestinal lesions The stomach is very rarely ulcerated but an atrophic gastritis may occur in advanced cases Fistula in ano and ischio rectal abscess are comparatively common complications and tubercle bacilli may be found in the discharges

e g there should not be marked acceleration of pulse or elevation of temperature except of very transient duration gastro intestinal disturbance or emaciation if present should not be excessive Obvious physical signs and radiological findings should be of very limited extent The physical signs should be either present in one lobe only and in the case of an apical lesion of one upper lobe not extending below the second rib in front or not exceeding an equivalent area in any one lobe or where these physical signs are present in more than one lobe they should be limited to the apices of the upper lobes and should not extend below the clavicle and the spine of the scapula Radiological findings should be limited to mottling involving a total area of not more than one zone No complications (tuberculous or other) of *prognostic gravity should be present A small area of dry pleurisy should not exclude* a case from this Group

Group 2—All cases which cannot be placed in Groups 1 and 3

Group 3—Cases with profound systemic disturbance or constitutional deterioration and with marked impairment of function either local or general All cases with grave complications whether they are tuberculous or not should be classified in this Group (*e g* diabetes tuberculosis of intestine or larynx)

Apart from the question of the expectation of life various stages of tuberculosis are described based upon anatomical lesions toxæmia and functional disablement

The course taken by tuberculosis of the lung may lead to several terminations These are (1) permanent arrest either by fibrosis prior to caseation or if the latter has occurred by calcification and fibrosis (2) incomplete arrest as shown by the persistence of tubercle bacilli in the sputum or by slight degrees of pyrexia on over exertion (3) rapid extension here the disease spreads and the toxæmia is out of all proportion to the extent of the lesions (4) death this may result from the pulmonary lesion or from complications The lesion may prove fatal as the result of progressive asthenia or cardiac failure from asphyxia due to acute miliary tuberculosis or hæmoptysis or in a small proportion of cases directly from loss of blood in repeated hæmoptysis The complications that most often prove fatal are meningitis enteritis laryngitis leading to dysphagia and starvation or pneumothorax Intercurrent diseases such as pneumonia influenza or diabetes are occasionally the cause of death

Prognosis —A number of factors must be critically considered in the determination of the prognosis in pulmonary tuberculosis

Rapid progress of the disease in other members of the family suggests a diminished familial resistance and therefore an unfavourable prognosis

Personal history —Chronic alcoholism is serious chiefly because the regime of treatment is then peculiarly irksome while the digestion and powers of resistance are often impaired in alcoholics The outlook is grave when tuberculosis is conjoined with diabetes though less so since the use of insulin Congenital heart disease and pulmonary stenosis are unfavourable factors but hypertrophy of the heart and mitral stenosis are said to be beneficial

The prognosis is very grave in infants and young children but slightly less serious up to the age of 20 Between 20 and 50 age has little influence but in later years the outlook becomes progressively less favourable

Apart from the effects of pregnancy and exposure sex plays no important part

Freedom from financial embarrassment improves the prognosis inasmuch as advice can be sought early and treatment carried through thoroughly

Marriage often leads to a breakdown in arrested cases especially in women and induces more rapid spread of active lesions

Persistence in an unfavourable occupation or return to it after completion of institutional treatment affects the prognosis adversely

Poor chest development and the habitus phthisicus are usually bad prognostic signs although tuberculosis may run a rapid course even in patients with good physique

It has also been used as a guide to prognosis since it is affirmed that arrest should not be considered as firmly established until the sedimentation rate has returned to normal This may not occur until some time after the usually accepted clinical symptoms and signs of activity have disappeared

THE TUBERCULIN TESTS —1 *Cutaneous* (*the Pirquet reaction*) —Scarifications are made on the skin of the forearm through a drop of Koch s old tuberculin, human or bovine and through a drop of saline as a control A positive reaction is shown by the formation of a slightly raised, reddened papule at the site of the scarification through one or other varieties of tuberculin, whereas the control is not affected Unfortunately except in the first 2 years of life this affords no indication of active disease, but only reveals the presence of previous infection with resulting tuberculin sensitiveness A positive reaction is therefore given by the majority of adults

2 *Mantoux s intradermal test* —An injection of 0 1 ml of a 1 in 10,000 dilution of old tuberculin (0 01 mg) is given intradermally If no reaction occurs, the injec tion is repeated in a week with 0 1 ml of 1 in 1,000 dilution (0 1 mg) If still negative 0 1 ml of 1 in 100 dilution may be used A positive reaction is shown by a red areola with some œdema of at least 5 mm in mean diameter after 2 or 3 days

A modification of this test consists in the use of Purified Protein Derivative (P P D) This is supplied in tablets of two strengths which must be dissolved in a buffered solution immediately before use The advantage of this preparation is its constant potency

3 *Vollmer s patch test* —A strip of adhesive plaster is applied over the sternum previously cleaned with ether To this strip are attached three small squares of filter paper the central one is a control of untreated paper, the other two have been saturated with undiluted old tuberculin and allowed to dry The plaster is removed in 48 hours and 12 or 24 hours later a positive reaction is shown by redness infiltra tion and sometimes by papules or vesicles

4 *Tuberculin jelly patch test* —The jelly which contains 95 per cent old tuber culin is squeezed out from a tube on to the skin between the shoulder blades which has been cleaned with acetone It is covered before drying with Elastoplast which is removed 48 hours later A positive reaction is shown by erythema with slight vesiculation This test is more accurate than the Vollmer test and gives as high a percentage of positives as does the Mantoux test

Course —The course pursued by pulmonary tuberculosis is variable depending upon the type of the disease In acute miliary tuberculosis before the use of strepto mycin, death could occur within a few days or weeks of the onset of symptoms In acute caseous tuberculosis death often follows in a few months In chronic fibro caseous tuberculosis the disease may be completely arrested or relapse at intervals in other instances it progresses steadily in spite of all treatment to a fatal termination In fibroid tuberculosis the disease may become completely arrested or smoulder gently for many years

CLASSIFICATION —That suggested by the Joint Tuberculosis Council has been adopted by the British Ministry of Health

Patients suffering from any form of tuberculosis should be divided into *Class A*—cases in which tubercle bacilli have never been discovered in any exudate excrement discharge or tissue (T B minus) *Class B*—cases in which tubercle bacilli have been found at any time in any exudate excrement discharge or tissue (T B plus)

The extent of the pulmonary lesion is best described by radiological zones as follows The upper zone—that area above a straight line running through the lower borders of the anterior ends of the second ribs The middle zone—that area bounded by the above line and one running through the lower borders of the anterior end of the fourth ribs The lower zone—the remainder of the lung below the middle zone

Respiratory cases in both Classes A and B should be further sub divided in three groups as follows *Group 1*—Cases with slight constitutional disturbance if any

deleterious effect Involvement of the genito urinary system increases the severity of the disease especially if the kidneys or bladder are affected If the epididymis alone is involved the prognosis is not materially affected as the lesion can be dealt with surgically although the administration of a general anæsthetic may cause spread of the pulmonary disease For this reason when operations are urgently needed on these patients gas and oxygen basal anæsthetics local or spinal anæsthesia should be insisted on

The rate of sedimentation of the erythrocytes (see p 1023) has proved to be a valuable aid to prognosis A persistently rapid rate is unfavourable

Treatment —PROPHYLACTIC —The prophylaxis of tuberculosis involves a consideration of public health questions dealing with the purity of the milk supply the inspection of meat sanitation and housing the early diagnosis of tuberculosis the examination of contacts and the segregation of ' open cases Inoculation with B C G vaccine (attenuated living bovine bacilli) is being used increasingly in Great Britain for protective vaccination of children and especially of contacts It is now generally advised for Mantoux negative reactors on hospital staffs All these questions are considered in the general article on Tuberculosis Mass radiography using miniature films has been used for investigating the incidence of unsuspected tuberculosis in certain groups of the population such as factory workers and men in the forces The average findings in this series shows that in about 0 5 per cent of those examined shadows suggestive of tuberculosis are found although the incidence of active disease is considerably lower If these cases can be adequately treated it should tend to check the spread of infection

The treatment of Mantoux negative reactors working in sanatoria or hospitals has recently received attention The Joint Tuberculosis Council advises that they should be weighed and have their blood sedimentation estimated monthly and their Mantoux reaction tested at least every 3 months preferably every month When the reaction becomes positive they should be examined radiologically and clinically According to the degree of the signs and the radiological appearances they may either be allowed to work part time and rest in bed when off duty or taken off duty till it is clear that no progressive lesions are developing Those showing definite symptoms must be treated as cases of active disease

CURATIVE —This varies with the type and stage of the disease In all acute or febrile cases treatment should be commenced at home or in a nursing home or hospital where the patient can be under careful observation in bed The various forms of treatment which may be considered are—(1) sanatorium treatment (2) home or institutional treatment (3) dietetic treatment and personal hygiene (4) climatic treatment, (5) graduated rest exercise and labour (6) medicinal treatment (7) specific measures (8) operative treatment (9) symptomatic treatment

1 SANATORIUM TREATMENT —This constitutes the best mode of treatment for early and for certain types of chronic disease but is totally unsuited for acute febrile or very active cases The advantages obtained are (*a*) the patient learns the most suitable mode of life and the methods employed to check the spread of the disease (*b*) the housing is specially designed and the climatic conditions are good (*c*) the dietary is abundant and adapted to the patient s needs (*d*) there is constant skilled medical supervision and the daily routine is adapted to the actual physical condition of the patient

On arrival a newcomer is kept in bed for a few days in order that his resting temperature may be observed and the necessary examinations carried out. If there is pyrexia rest in bed must be enforced until the temperature falls to normal If the temperature rises above 99 F when the patient is up return to bed is usually necessary The routine of sanatorium treatment varies in different institutions the most important divergence being whether or not a system of graduated exercise is employed In nearly all an hour s recumbent rest is enforced before lunch and dinner

Patients with resolute and persistent personality are more likely to persevere with treatment and to recover than those of weaker moral fibre

The prognosis is greatly affected by the type of the disease Acute miliary tuberculosis used to be rapidly fatal in 100 per cent of cases, whereas with the use of streptomycin the mortality is less than 50 per cent and in acute caseous tuberculosis although the prognosis is very grave, recovery may occur In fibro caseous tuberculosis the prognosis is most uncertain and difficult to forecast Every factor must be carefully considered and the response to treatment noted The best outlook is in fibroid disease, which often undergoes complete and permanent arrest

SYMPTOMS IN THEIR RELATION TO PROGNOSIS —Persistent cough, by exhausting the patient and disturbing sleep, is often unfavourable

The amount of sputum is usually dependent upon the type of disease and upon the presence of secondary infection and may therefore be of value in prognosis.

The significance of tubercle bacilli in the sputum —The figures obtained at the Midhurst Sanatorium, over a period of 8 years in which the after-history of the patients was traced for the ensuing 6 years, show that the prognosis is best in closed' cases, but that it is nearly as good in those cases in which the tubercle bacilli disappear from the sputum during the sanatorium treatment Persistence of bacilli in the sputum is an unfavourable sign The actual number of bacilli in the sputum and the presence of beading' have no definite prognostic significance

Cases commencing with hæmoptysis progress more satisfactorily than those with other modes of onset, chiefly because they are diagnosed earlier Hæmoptysis occurring later may exert an unfavourable influence either indirectly by spreading the disease into previously healthy portions of the lungs or actually by the loss of blood

If dyspnœa is not due to attacks of bronchial spasm, it has usually an unfavourable significance

The temperature affords a clue to the type and activity of the disease, and is thus a valuable aid to prognosis Profuse and persistent night sweats or marked anorexia especially when occurring early in the disease are grave signs Tachycardia due to toxæmia, signs of cardiac failure œdema and albuminuria are of bad omen The blood pressure is thought by some to be a useful guide, systolic figures below 100 mm Hg being unfavourable, whereas a rise of pressure may be associated with amelioration of the disease In fibroid lesions the pressure may be raised throughout.

THE EXTENT OF PHYSICAL SIGNS —The activity of the disease rather than its extent is often the more important factor in determining prognosis but both factors are of importance since the outlook is always more serious if both sides are affected especially if cavitation is present The development of compensatory emphysema is of value only as an indication of fibrosis in the tuberculous portion of lung and therefore of chronicity

THE INFLUENCE OF COMPLICATIONS ON PROGNOSIS —Generally speaking, the presence of complications increases the gravity of the disease Involvement of the larynx is a serious complication especially when accompanied by dysphagia but complete recovery may take place if the pulmonary lesion is quiescent In early cases spontaneous pneumothorax occasionally acts favourably, but when it develops in association with extensive tuberculosis and especially if it progresses to pyopneumothorax it is almost invariably fatal though, if the disease is unilateral, surgical measures may prove successful

Pleural effusion often has a beneficial influence by diminishing the movements of a lung in which there is an early tuberculous focus

Secondary catarrhal affections tend to increase the cough and expectoration and may lead to further spread of the disease

Meningitis is still a very serious complication but streptomycin has made a great difference to the prognosis Tuberculous peritonitis or enteritis is a very grave complication but fistula in ano often occurs in chronic cases and exerts no marked

culous toxins and that if the exercise was carefully graduated a condition of increasing immunity through the use of autogenous tuberculin would arise However even if the theory has no certain foundation and excess effort is to be avoided, progressive occupational therapy is essential

6 MEDICINAL TREATMENT —There has been a long series of drugs used in the treatment of tuberculosis One no longer used which had a long vogue and an extensive optimistic literature was sanocrysin It took over 10 years before it fell into virtual disuse because the natural course of pulmonary tuberculosis is so uncertain that it takes a great many years and a great many cases before one can conclude any thing from studying the results of treatment

Streptomycin starts with the very great advantage that it is known to cure many cases of two diseases previously incurable miliary tuberculosis and tuberculous meningitis In pulmonary tuberculosis it is thought to be most effective where there is fresh infiltration and less so or ineffective in chronic fibrocaseous tuberculosis

Streptomycin is usually given in doses of 1 g daily It may be given continuously over a period of 2 or 3 months at a time but it is more usual to give two to four courses of injections each lasting 2 or 3 weeks with an interval of about 2 weeks between each course The object of the interval is to diminish the likelihood of toxic reaction One of these is giddiness due to labyrinthine damage Another is nerve deafness which sometimes follows the prolonged dosage given in miliary tuberculosis or tuberculous meningitis A less common toxic reaction is an urticarial or erythematous rash with or without pyrexia The effectiveness of streptomycin is limited by the tendency for drug resistance to develop The organisms rarely become resistant before a minimum period of 14 days but the number of resistant strains rapidly rises in proportion until after about 3 months it is maximal unless measures are taken to prevent it It has been found that the simultaneous administration of other drugs such as sodium aminosalicylate (P A S) or isoniazid diminishes or delays the appearance of strains resistant to streptomycin or to themselves

Streptomycin in combination with one or other of the above drugs is given generally in cases of miliary tuberculosis or tuberculous meningitis It is usually given in acute caseous pneumonia or broncho pneumonia

Physicians differ as to its use in other forms of the disease Many oppose its use in fibrocaseous disease because it is not very effective because the patient may spread streptomycin resistant disease and because if the patient subsequently requires surgery it would probably not be possible to get a maximal effect in the prevention of local spread of infection during surgical intervention On the other hand it may serve to prevent or limit the local spread of broncho pneumonia which bring the patient s life progressively to an end Some use it in tuberculous pleural effusion or in minimal tuberculous lesions in an attempt to arrest the disease in its incipient stage They discount the possibility of losing the eventual protective effect of streptomycin by the hope that they will have rendered improbable the necessity of surgical intervention Many use it in early infiltration with the same object It is rarely given in *primary* tuberculosis although it is probably wise to give it in very young children or in the so called progressive primary in which a massive primary lesion slips directly into a post primary stage with incidental danger of miliary spread It is generally used to prevent spread during resection or thoracoplasty

It appears to be effective in the treatment of tuberculous laryngitis tuberculosis of the bronchi ulcers of the tongue and possibly of the intestines

The permanent place of streptomycin in therapy will take many years to determine Sodium aminosalicylate has a bacteriostatic effect *in vitro* but is not apparently bactericidal It has been used by itself in treatment and good results have been claimed Probably its only important use is in combination with streptomycin to delay the development of resistant strains of tubercle bacilli The dosage recommended is 3 to 4 g four times a day making a total daily dosage of 14 to 18 g Large

After 3 months stay it is usually possible to decide whether the patient is responding to treatment, and if so it should if possible, be prolonged for at least another 3 months or until the sputum is free from tubercle bacilli

2 HOME AND INSTITUTIONAL TREATMENT —Treatment at home in nursing homes or in special hospitals is essential in early cases with fever and in cases in which it is necessary to establish the diagnosis Home treatment is also usually necessary on return from sanatorium or climatic treatment, if arrest is incomplete An endeavour should always be made to carry out the principles inculcated at the sanatorium and the patient should be under regular medical supervision Advanced cases are best looked after in special institutions

3 DIETETIC TREATMENT AND PERSONAL HYGIENE —It is desirable to graduate the diet in each case so that the *patient is restored to the previous maximum* weight but in order to accomplish this, the food should be slowly increased and all ideas of enforced overfeeding discountenanced A total calorie value of 3000 to 3500 is usually ample but, if the patient is performing heavy work as much as 4000 may be necessary Meat, fish, eggs and fats are usually well tolerated It is not often necessary to give large quantities of milk when the patient is on a full dietary

In all cases in which there is expectoration the patient should be clean shaven Great care must be taken in the disposal of sputum to ensure that it does not become dry and that flies do not have access to it All patients who are up should carry special sputum flasks while those who are in bed should have sputum cups suitably covered and containing disinfectant The sputum should be burnt, or, if this is impossible it should be emptied into the water closet after disinfection with carbolic acid or other simple or cheap disinfectant

Smoking is best avoided in cases of active disease or laryngeal tuberculosis and in no instance should inhaling be allowed Sun bathing and injudicious uncontrolled sun exposure are dangerous and often activate quiescent lesions Patients should be strongly warned of this danger

4 CLIMATIC TREATMENT —Climate is not now considered to be so important as it used to be Broadly speaking, bracing areas with cool dry air, porous soil and moderate height promote a feeling of well being stimulate the appetite and the mind and are more favourable than damp low lying relaxing sites Countries with a high mean temperature and high humidity are unsuitable for tuberculous patients With proper treatment patients are just as likely to recover in the sanatorium in their home area as by travelling far afield There is no special virtue in Switzerland except that the mountains are an agreeable background to prolonged bed rest and the air and atmosphere are crisper and cleaner than in this country In any case early treatment and control are best carried out in this country Patients with diminished vital capacity due to fibrosis or emphysema should not be sent to sanatoria at over 2 000 ft

5 GRADUATED REST AND EXERCISE —Rest is an essential preliminary part of the treatment of active tuberculosis Even apyrexial patients benefit from several weeks of bed rest Pyrexial cases must be kept in bed until the temperature has remained normal for several weeks It is an advantage to allow patients up for toilet purposes but acute cases with a high initial temperature may require periods of absolute rest when no movement or activity on the part of the patient is allowed Rest treatment should be controlled by careful temperature observations Rectal temperatures or 5 minute mouth readings must be used and even minor variations should be regarded as significant

The patient is allowed to get up by degrees starting with 1 hour daily increasing to 6 or 8 hours If still apyrexial the patient is allowed walking exercise of 1 or 2 miles daily The system of graduated exercise which Paterson instituted at the Frimley Sanatorium caused a revolution in sanatorium treatment in that it introduced a progressive occupational therapy into the previously otiose and sterile stagnation of sanatorium life Paterson had the theory that muscular exercise *liberated tuber-*

invariably occurs and the treatment by artificial pneumothorax cannot be repeated In some cases of bilateral disease which is active but not very extensive in either lung a cautious use of bilateral artificial pneumothorax has proved practicable and helpful but very great care is necessary in adjusting the pressures

There are certain dangers in the procedure These are now rare, and they can usually be prevented by careful attention to the technique Death has occurred from air embolism when the needle has accidentally been put into a blood vessel in the lung It is for this reason that air should never be allowed to flow unless there is a clear negative swing of the manometer showing that the needle is in the pleural cavity If the lung is adherent to the chest wall owing to pleural adhesions or if the needle is pushed in too far it may be inserted into the lung or into a pulmonary cavity the manometer will then show a swing above and below the zero line instead of entirely below it. Under these circumstances no air should be allowed to enter The needle may be inserted into a blood vessel In this case the manometer pressure will rise above zero and blood may appear in the glass section inserted in the rubber tube leading from the manometer to the needle The needle should be withdrawn immediately lest air should enter the vessel

If the pleura is found to be adherent at the site of the first puncture another attempt may be made elsewhere *e g* just below the inferior angle of the scapula This spot may be selected for the initial puncture in left sided cases where there is marked cardiac displacement In cases in which localised band or cord adhesions prevent adequate collapse it is often possible to cut them by electrocautery or dia thermy through an operating thoracoscope thus ensuring completely effective collapse. This is called internal pneumolysis Provided that the lung is sufficiently relaxed to permit closure of cavities the persistence of adhesions does not necessarily make the treatment ineffective

Over-collapse may lead to atelectasis of a lobe probably due to bronchial obstruction It is not uncommon after adhesion section Its persistence is a serious complication as it may lead to pleural effusion empyema or bronchiectasis but often the lung re-expands as the excess air is absorbed Pleural effusions sometimes occur during treatment Small amounts of fluid in the costophrenic gutter occur at some time in the majority of cases Large effusions sometimes occur requiring aspiration They do not necessarily prevent continuation of treatment but are often followed by progressive obliteration of the pleural cavity and occasionally they become purulent

Other rare complications are pressure pneumothorax following injury to the lung during induction or refill and very rarely secondary infection of the pleural cavity

(*b*) *Phrenic paralysis* —Crushing of the phrenic nerve results in a paralysis lasting from 8 to 18 months The paralysed diaphragm is elevated at rest and rises during inspiration The degree of collapse varies very much but occasionally very satisfactory lung relaxation occurs It is rarely used as the only treatment but is usually combined nowadays with pneumoperitoneum

The indications are the same as those for pneumothorax and it is used where pneumothorax has failed or is being postponed for some reason Phrenic crush should not be used if thoracoplasty is likely to be necessary as the operation cannot be performed until the diaphragm recovers its mobility Occasionally phrenic crush is followed by permanent paralysis

(*c*) *Pneumoperitoneum* —Air introduced into the peritoneal cavity raises the dia phragm and produces partial collapse of the bases of the lungs As in an artificial pneumothorax the injections of air must be repeated at intervals to compensate for absorption In order to achieve the best results, the diaphragm on the affected side should be paralysed by crushing or evulsion of the phrenic nerve In a favourable case a pneumoperitoneum will raise the diaphragm by several inches and this, together with the abolition of the diaphragmatic movement, relaxes and rests the lower part of the lung The operation is indicated in cases of cavitating tuberculous

doses have been used but they often produce gastric disturbances which may necessitate the abandonment of the treatment, and the doses given above are usually the largest that can be tolerated by the majority of patients Small initial doses and the routine administration of the drug with meals often limit the gastro-intestinal disturbances The drug may produce erythematous rashes with pyrexia in a small percentage of cases

Isoniazid (isonicotinic acid hydrazide) is also used in the treatment of pulmonary tuberculosis, the usual dose being 100 mg in the morning and 50 mg in the evening but it may be increased to a total of 200 mg per day in divided doses It is bactericidal *in vitro* and good results are obtained in treatment with this substance combined with streptomycin Resistance to isoniazid develops rapidly but appears to be delayed when it is combined with streptomycin and there seems to be some probability that it delays the development of streptomycin resistance as effectively as does sodium aminosalicylate Its status in the treatment of pulmonary tuberculosis cannot be finally estimated at the present moment

The sulphones and thiosemicarbazones are of doubtful value, and liable to produce methæmoglobinæmia and anæmia in the first instance and jaundice and possible liver damage in the second

7 COLLAPSE THERAPY—This form of treatment has the object of relaxing the affected lung and allowing it to contract towards the hilum In this way it provides rest allows cavities to collapse and therefore heal and probably prevents the spread of tuberculous disease in the collapsed lung and prevents the formation of cavities

The following methods of collapse therapy are available—artificial pneumothorax, phrenic paralysis pneumoperitoneum extra pleural pneumothorax and thoracoplasty

(*a*) *Artificial pneumothorax*—This treatment is the oldest method of collapse therapy, dating from Forlanini of Pavia in 1898 In suitable cases it is still the most effective method of collapse therapy

If old and dense pleural adhesions are present, it is impracticable If there is much emphysema or cardiac embarrassment it involves risk It is also of value in certain cases of repeated severe hæmoptysis Tuberculous laryngitis or enteritis are not contraindications providing that other conditions are suitable Sterile air is introduced into the pleural cavity and the lung allowed to collapse The method of induction of artificial pneumothorax is as follows A preliminary subcutaneous injection of gr $\frac{1}{3}$ of papaveretum (Omnopon) is given half an hour before the start. The patient lies on the sound side with the head low and supported on a pillow A second pillow is placed under the chest to expand the intercostal spaces The skin and the tissues down to the pleura are anæsthetised with 2 per cent procaine hydrochloride solution after the application of iodine The site usually chosen is in the sixth intercostal space in the mid axillary region The pneumothorax apparatus is carefully tested to make sure that it is in working order A special pneumothorax needle is attached to the machine by a rubber tube which is pinched to show that the manometer oscillations are free and the needle is then pushed through the intercostal space until the pleural cavity is reached The apparatus is then adjusted so that the intrapleural pressure can be observed No air should be introduced until the manometer shows a normal negative pressure range with inspiration, of 5 to 10 or more cm of water This is the test of entry into the pleural space and when this is established 200 to 300 c cm of sterile air may be allowed to enter the pleural cavity The final pressures are then recorded and the needle is withdrawn A refill is given next day and another after 2 more days the quantities of air introduced being determined by the final pressures which should be kept slightly negative Subsequent refills are gradually spaced out to a week, then 10 days and later to 2 3 and 4 weeks intervals The usual custom now is to maintain the collap e for 3 years or longer If the condition of the patient is satisfactory re expansion may then be permitted cautiously It should be remembe ed that after expansion pleural adhesion almost

is rarely fatal except in advanced cases but causes alarm out of proportion to the danger Reassurances and sedatives help to allay fear but sedatives should be adapted to circumstances and not overdone If the bleeding is severe and continual drip transfusion should be given

Artificial pneumothorax has been used to stop hæmorrhage when the affected side is known although it is rarely needed and indeed it is probably seldom that it could be performed It has however been successfully employed on several occasions when all other measures had failed

Congo red and other blood coagulants are of no value

Gastro-intestinal symptoms—Anorexia or dyspepsia are usually due to toxæmia and improve with rest Sometimes the milk diet increased fat cod liver oil and so forth which these patients are often given are the cause of the dyspepsia Alkalis are often helpful Patients should be advised not to swallow their sputum and told why they should not as otherwise they often ignore this advice

If diarrhœa develops a low residue diet with a high vitamin content should be given Diarrhœa usually occurs in terminal cases and tincture of opium will help to relieve it.

Insomnia is often a troublesome symptom and every endeavour should be made to obtain a good night s rest by administration of mild hypnotics and by relieving distressing cough and pain

The treatment of the complications of pulmonary tuberculosis is described under their respective headings The rehabilitation of patients discharged from sanatoria is an important subject to which considerable attention is being devoted and involves a consideration of the advisability of establishing training centres or industrial colonies for consumptives These are proving of very great value

MINIMAL TUBERCULOSIS

As a result of mass radiography the significance of minimal lesions requires especial study There are various definitions of what constitutes a minimal lesion but the exact definition is not important

These are usually small nodular discrete lesions found in the upper part of either lung usually below the first or second or third ribs there may be one or more than one they do not give rise to any physical signs and their presence can only be detected by radiological examination These are post primary lesions and are not accompanied by glandular enlargement. Under observation these shadows may rarely recede and disappear or may become denser as they are replaced by fibrous tissue or calcification They may on the other hand eventually cavitate or there may appear in the adjacent lung small areas of infiltration with progressive disease These latter changes may occur months or more often years after their first detection

Observation has now shown that at least 30 per cent develop into progressive disease and the proportion may really be higher At the present time partly owing to shortage of hospital and sanatorium accommodation in many clinics patients showing these radiological shadow are merely kept under observation without treatment only receiving treatment when progressive disease has occurred It is probable that most cases of progressive tuberculosis with sputum would at some time previous have shown these minimal lesions These lesions should always therefore be treated seriously as they present a golden opportunity for treatment at an early stage If successfully treated progressive tuberculosis might become rare and the incidence of tuberculosis diminish

It has already been stated that some of these lesions become calcified and give no further trouble but there is at the present time no method of determining which lesions will remain static and which will progress Patients showing these lesions

lesions in the lower lobe when an artificial pneumothorax has failed It is particularly successful in the treatment of cavities in the apex of the lower lobe (dorsal segment) Care is necessary in the technique to avoid the risk of air embolism This treatment is used where pneumothorax has failed or as a prelude to pneumothorax treatment when the activity of the tuberculous disease in the lung has subsided sufficiently to make pleural effusion less likely to follow artificial pneumothorax It is less effective than pneumothorax treatment but quite effective in some cases

(*d*) *Extra pleural pneumothorax* —This treatment was the logical development of pneumothorax treatment when it was impossible to collapse the lung by orthodox pneumothorax treatment on account of adhesions Collapse is obtained by separating the pleura and the underlying lung from the chest wall inside the endothoracic fascia and then by maintaining the separation by putting air in the space thus formed It fell out of use because of the frequency of secondary infection and spread of disease to the extra pleural space The development of antibiotics has led to some revival of the operation

(*e*) *Thoracoplasty* —This operation was originally used in cases where artificial pneumothorax had been attempted and failed because of adhesions or because cavities remained patent in the partially collapsed lungs It is however, often used as a primary form of collapse It is particularly used to collapse apical cavities The operation involves division of a variable number of ribs sometimes combined with apicolysis to allow the lung to collapse by mobilisation of the chest wall It is a serious operation but good results are obtained The more radical thoracoplasties are not so often done nowadays and resection is replacing many thoracoplasties

(*f*) *Resection* —All the surgical measures previously described are designed to put the diseased lung in a favourable state for natural healing to occur Resection aims at eradicating the lesion itself It is a less mutilating operation than thoracoplasty and more effective than thoracoplasty in dealing with cavities of the lower lobe It is being increasingly used to remove apical cavities tuberculomata and tuberculous bronchiectasis Only time can show whether too optimistic a view is taken of its value by some enthusiasts Its use is limited by the multiplicity of tuberculous lesions Resection may very well replace many forms of collapse therapy but its least debatable value at present is in putting a full stop to disease already arrested by other methods No form of surgical treatment is a substitute for general treatment

8 Symptomatic Treatment —When cough is ineffective it may be relieved by a sedative lozenge or linctus containing diamorphine or codeine or by the well known liquorice lozenge If there is difficulty in bringing up the sputum a simple saline mixture is of value such as sodii bicarb gr 10, sodii chlorid gr 3 sp chlorof min 10 and aq anethi dest ad fl oz 1

Night sweats —Free ventilation is the key to prevention The windows should be widely open The clothing and bedclothes should be as light as consistent with warmth Feather or rubber mattresses should be avoided In very severe cases a rush or thin cork mattress has been recommended

Fever —Rest in bed up to the extent of absolute rest is the best means of lowering the temperature

Hæmoptysis —In cases in which the sputum is only streaked no special treatment is required Moderate hæmoptysis with expectoration of 3 or 4 oz of blood requires more active measures The patient should be put to bed and as there is usually anxiety given a sedative either chloral hydrate or morphine gr ⅛ In profuse or persistent hæmoptysis the patient should be confined strictly to bed and if it is known from which side the bleeding has occurred he should be on the affected side to prevent the blood from being aspirated into the sound lung

He should have one or two pillows and should not be kept too immobile as the blood may cause collapse of one or more lobes unless it is coughed up Hæmoptysis

Symptoms—These are in general identical with those of the chronic forms of pulmonary tuberculosis such as cough, expectoration, which may be offensive, dyspnœa fever and night sweats.

Complications and Sequelæ—These are usually due to the other localisations of the organism but in addition empyema and bronchiectasis may be mentioned

Diagnosis—This can only be established by the discovery and identification of the organism in the sputum and the discharge The characteristic "sulphur grains are not invariably present and may escape notice unless looked for carefully In any obscure case of pulmonary disease in which tubercle bacilli are not found after repeated search the possibility of actinomycosis should be considered and direct films should be specially examined

Course—This is progressive and may lead to asthenia emaciation and death

Prognosis—This is serious although some cases respond well to treatment.

Treatment—(See p 196) Surgical treatment of local abscesses or of empyema may be required Penicillin is often effective in doses of 1 million units daily for several weeks Large doses of potassium iodide are traditional

PULMONARY ASPERGILLOSIS

Ætiology—Infection of the bronchi and lungs sometimes occurs by *Aspergillus fumigatus* more rarely by *A nidulans* The disease has been most frequently observed in France It occurs among pigeon breeders and hair sorters and combers The former acquire the disease from the process of artificial feeding from transferring grains in the mouth to the beak of the bird the latter from the use of rye flour in cleaning the hair Millers and farm labourers have also been the subjects of the disease

Pathology—The fungus induces nodular formations in the lung tissue somewhat resembling aggregated tubercles Bronchitis patchy lobular consolidation and fibrosis result Emphysema bronchiectasis and cavity formation may follow A secondary aspergillosis may occur in chronic cases of bronchitis or lung disease but is of little clinical importance

Symptoms—Primary aspergillosis produces symptoms similar to those of bronchitis broncho-pneumonia or pulmonary tuberculosis according to the localisation and degree of the lesions The sputum may be blood stained or definite hæmoptysis may occur There is generally wasting with irregular fever

Diagnosis—The condition has to be differentiated from pulmonary tuberculosis and from other varieties of pneumonomycosis It may be suspected when repeated examinations of purulent sputum do not show tubercle bacilli It is however a rare disease and even if the fungi are found they may be secondary invaders or contaminants

Course—Acute broncho pneumonic forms may be fatal in a few weeks or months The chronic lesions may extend to years and arrest with fibrosis is not uncommon

Treatment—This consists in avoiding further infection and giving large doses of potassium iodide Open air measures and general tonic treatment are also to be recommended All Aspergilli are completely resistant to penicillin

FARMER S LUNG (see p 1015)

OTHER MYCOTIC INFECTIONS

Fungi of the genera *Blastomyces* (*Oidium Coccidioides*) and *Sporotrichum* are well known to produce cutaneous affections simulating chronic gummatous or tuberculous lesions They may also give rise to pulmonary disease producing symptoms like those of tuberculosis

should be put to bed Five minute or rectal temperatures should be carefully charted and the sputum, if any, should be examined, if there is no sputum laryngeal swabs or gastric washings should be examined and cultivated, although at this stage tubercle bacilli are rarely found Observation of the temperature chart will often show minor yet important deviations from the normal, even in patients who have no symptoms A raised sedimentation rate should be accepted as evidence of activity, but the sedimentation rate is rarely raised and a normal sedimentation rate does not exclude a progressive lesion If all these observations are negative it may be considered safe to discharge the patient and keep him under observation A wiser course however is probably to give these cases courses of streptomycin and isoniazid Whether progressive disease can be prevented by this treatment it is not yet possible to say but certainly it does not always prevent spread of the disease Artificial pneumothorax does appear to prevent spread and cavitation and should be induced in young patients or patients who show definite evidence of activity as shown by pyrexia a positive sputum or radiological change in the lesion In the United States of America these lesions are often excised and incidentally it has been shown that they represent a localised broncho pneumonia Resection may well become the treatment of choice but the difficulty of adopting drastic measures of treatment or even of admitting the patients for observation and assessment is that the patient has no symptoms whatever The name minimal lesion is not a happy one, as it suggests an insignificant lesion but once it is generally realised that these shadows like the cloud no bigger than a man's hand may be the presages of storms to come, they will receive the serious treatment which they deserve and the whole picture of pulmonary tuberculosis may be altered in our own time

THE PULMONARY MYCOSES (PNEUMONOMYCOSES)

A number of fungi produce pulmonary lesions Considerable confusion exists in regard to their nomenclatures, and at the present time it is difficult to give accurate accounts of them The pulmonary mycoses have one feature in common in that they produce chronic pulmonary lesions practically indistinguishable clinically from those of the chronic forms of pulmonary tuberculosis

Among the varieties of mycotic infection at present separated clinically may be mentioned—Actinomycosis, Sporotrichosis (see p 196) Aspergillosis Torulosis (see p 197) North and South American Blastomycosis (see pp 198, 199), Coccidioidosis (see p 200), and Histoplasmosis (see Appendix *i*)

PULMONARY ACTINOMYCOSIS

Ætiology —The general characters of the streptothrix group of organisms are described in the section on Actinomycosis (see p 193) A large proportion of cases show the first lesions in the head and neck regions but primary pulmonary cases occur and are probably more frequent than is generally recognised

Pathology —In the primary pulmonary cases the distribution of the lesions is at first very similar to that of tuberculosis and the disease may extend in an identical manner In the forms due to spread from other organs such as the liver the base of the lung may be first involved while in cases extending down from the neck the path of the infection is apparent

Owing to the tendency of the lesions to spread by contiguity subcutaneous abscesses may form and simulate caries of the ribs Pleural adhesion is the rule but occasionally empyema results When a subcutaneous abscess ruptures or is opened the characteristic sulphur granules may be found although this is not invariable The skin around the sinuses which result is often puckered in a somewhat characteristic fashion

bronchi may complicate the course Bronchiectasis has already been mentioned and tuberculosis may occur as a complication

Diagnosis —This is often difficult and sometimes inconclusive Obscure pulmonary signs in a syphilitic subject should arouse suspicion The Wassermann reaction should be determined and other indications of syphilis looked for in all fibrosing and destructive lung conditions when no tubercle bacilli are found in the sputum These cases have never been common in modern memory and are becoming rarer Other syphilitic lesions such as aortic regurgitation are usually present. The difficulty of diagnosis is increased by the association of syphilis and tuberculosis mentioned above

Course and Prognosis —Where the lesions are localised and can be recognised early the course is favourable if anti syphilitic treatment is applied Where fibrotic changes occur leading to bronchiectasis the course is less favourable and in the destructive form it is serious An inter-current tuberculous infection increases the gravity of pulmonary syphilis

Treatment —When a diagnosis of pulmonary syphilis has been established vigorous anti syphilitic treatment should be carried out Its beneficial effect is undoubtedly promoted by open air treatment In cases where tuberculosis coexists with syphilis anti syphilitic treatment is strongly recommended especially by French physicians

NEW GROWTHS IN THE LUNGS

Both benign and malignant tumours may occur in the lungs the latter being the more common

Ætiology —Malignant tumours occur more frequently in the male sex in the ratio of 5 to 1 carcinoma is rare before the age of 40 The lung is now the commonest site of cancer in the male Some of the apparent increase is due to more accurate diagnosis but there is probably a genuine increase It has been observed that cancer of the lung is most commonly found in smokers and Doll and Hill have produced suggestive figures showing that heavy cigarette smokers have a much greater incidence than non smokers Further studies are necessary to determine the importance of cigarettes as an ætiological factor

Pathology —Benign tumours found in the lungs usually arise in the bronchial mucous glands or in the bronchi They include adenoma fibroma lipoma and chondroma (see p 972)

Malignant tumours may be primary or secondary The primary growths are carcinoma or sarcoma It is probable that all varieties of bronchial carcinoma arise in the basal cells of the bronchial mucous membrane Certain types are described the squamous celled carcinoma the adeno or columnar celled carcinoma and the oat celled tumour The squamous celled carcinomata form a clearly differentiated group in which may be included columnar celled growths with duct and acinar formation the remainder are sometimes known as undifferentiated tumours consisting of more primitive types of cells These types however may be combined so that any one particular carcinoma may vary histologically in different areas Sarcoma is extremely rare and most tumours thus described prior to 1928 were in fact anaplastic carcinomata Metastatic carcinoma may arise from primary tumours in *breast stomach intestines liver pancreas prostate or kidney* and metastatic sarcoma most often results from tumours of bone Chorion epithelioma also give rise to secondary deposits in the lungs

Primary malignant tumours are usually unilateral but secondary growths are often multiple Dissemination in the lungs may occur by spread through the bronchi or vessels and a condition of miliary carcinomatosis is at times produced The pleura is often affected by direct extension Infiltration of or pressure upon the mediastinal structures frequently occurs

Castellani has described various broncho pulmonary conditions due to species of the genus *Monilia* (*Candida*) including the "tea tasters' cough" and "tea factory cough" Another fungus *Mucor mucedo*, has been found in the sputum, and is regarded as pathogenic to man

All these moulds produce bronchitic symptoms and mild infections while more severe forms simulate pulmonary tuberculosis The diagnosis in each case depends upon the recognition of the fungus, and the treatment recommended is large doses of potassium iodide

PULMONARY HISTOPLASMOSIS

This is described in the article on Histoplasmosis (see Appendix *i*)

TOXOPLASMOSIS

This is described in the article on Toxoplasmosis (see Appendix *v*)

SYPHILIS OF THE LUNGS

Ætiology—Clinically recognisable pulmonary syphilis is a rarity, but syphilitic lesions occur in the lungs in both the congenital and acquired forms of the disease

Pathology—Even post mortem it is often difficult to establish the syphilitic nature of the pulmonary lesions found in cases of syphilis owing to the fact that they tend to the formation of scars presenting no characteristic features

Congenital syphilis—The essential changes are—(1) Round celled infiltration with eventual fibrosis, starting round the bronchi and spreading to the inter alveolar framework, (2) periarteritis of the smaller arteries and (3) desquamation and de generation of the epithelium of the alveoli and bronchi Gummata may be present, but are rare Spirochætes can be demonstrated in the lesions by Levaditi s method The microscopic appearances comprise the "white pneumonia" of Virchow and an interstitial pneumonia which is commoner although both conditions are fre quently associated White pneumonia is found in premature or still born infants and in those dying soon after birth The condition may be widespread or localised The affected areas are firm consolidated smooth and greyish white in colour There are no interstitial changes, and the consolidation is due to the filling of the alveoli with desquamated degenerating epithelial cells

In the commoner interstitial form the lung is firmer harder and darker grey in colour and the connective tissue is mainly involved To this condition the term "pancreatisation of the lung" has been applied by Rogers

Acquired syphilis—Syphilitic lesions of the bronchi have already been described in the section on diseases of the bronchi Gummata may occur in or around the intra pulmonary bronchi or in the lung tissue They may be single or multiple and vary in size from that of miliary granules to a hen s egg They are said to be more common in the deeper parts of the lung near the roots and in the lower lobe They undergo changes similar to those occurring in gummata elsewhere but tend more to fibrosis and contraction than to softening Owing to these secondary changes the following conditions may result broncho pneumonic processes widespread fibrosis and con traction with pleural adhesion bronchiectasis and occasionally excavation

Symptoms—Small gummata may be latent and give rise to no symptoms or signs When fibrosis occurs they are similar to those of pulmonary fibrosis from other causes It is generally recognised that in rare cases a destructive process occurs formerly called "syphilitic phthisis" and almost exactly similar in its clinical mani festations to those of caseous or fibro caseous tuberculosis

Complications and Sequelæ—Syphilitic lesions in the larynx trachea or

pathy there is a progressive atrophic paresis predominantly affecting the limb girdles bulbar palsy diplopia and ptosis may occur the tendon jerks are diminished or absent there are often subjective sensory manifestations such as pain cramps or paræsthesiæ but objective sensory changes are rare

Diagnosis—This is difficult in early cases and not easy in some advanced ones It not infrequently happens that metastases especially in brain or bone, afford the earliest manifestations to be recognised Difficulties may arise in connection with pulmonary tuberculosis fibrosis and gumma of lung aneurysm pericardial and pleural effusion and enlargement of the mediastinal glands due to Hodgkin s disease or tuberculosis The whole body should be searched for evidence of malignant disease elsewhere The sputum should be examined repeatedly for tubercle bacilli and for cellular elements and a radiographic examination made of the chest Localised pulmonary collapse thus demonstrated may be a very early indication By the stereoscopic method excellent evidence of pulmonary neoplasms is often obtainable Lipiodol injection and radiographic examination or tomography may demonstrate the obstruction of a bronchus by the growth which often presents a tapering or rat tail appearance Bronchoscopy is essential in the diagnosis of bronchial carcinoma Temporary artificial pneumothorax may be helpful in diagnosis particularly in differentiating simple tumours in the periphery of the lung growths in the mediastinum and in the chest wall

The Pancoast tumour may give rise to special difficulty It has to be differentiated from syringomyelia cervical rib apical pulmonary tuberculosis and secondary sarcoma

Course—This is progressive the patient gradually losing strength and dying from cachexia or some intercurrent affection

Prognosis—Apart from those cases in which early recognition may in suitable conditions render lobectomy or pneumonectomy with removal of the growth possible this is hopeless death occurring in a few weeks or being delayed for 2 or 3 years The possibility of a successful pneumonectomy is more favourable with differentiated than with undifferentiated types of growth In the latter the growth tends to be more *infiltrating* and the glands are more likely to be involved

Treatment—Benign tumours are often capable of complete removal with gratifying success

In malignant growths lobectomy or dissection pneumonectomy with complete removal of the growth is only practicable for cases recognised early in which there are no secondary deposits

Radiotherapy may be useful by diminishing local pressure and relieving symptoms but cure by this method is rare

Useless cough should be checked by sedative lozenges or a linctus Dyspnœa due to pleural effusion may be relieved by tapping with or without air replacement but the fluid often reaccumulates rapidly Pain should be relieved by analgesic drugs and in the later stages those containing opium or its alkaloids may be required

TROPICAL DISEASES OF THE LUNG

Paragonimiasis or Distomatosis—Paragonimiasis is a disease contracted in parts of Korea Japan Formosa or China by bathing in or drinking infected water or eating raw crabs or crayfish The symptoms of cough hæmoptysis and pleurisy are caused by the invasion of the lung by flukes

Pulmonary Schistosomiasis—This disease is found in North and South Africa and particularly in Egypt It also occurs in South America and the West Indies It is caused by the invasion of the lung by the ova of *S hæmatobium* or *S mansoni* The ova form tubercles and there is an obliterating endarteritis of the arterioles

Symptoms —Simple tumours except adenomata are pathological curiosities, and as a rule only produce symptoms when they cause obstruction of a bronchus or press on mediastinal structures (see pp 972 1094)

The early symptoms of malignant growths are slight, and consist of malaise with, perhaps, cough and expectoration Later when the growth becomes more extensive and exerts pressure on or involves the larger bronchi, mediastinum or pleura, they are more noticeable Pain, dyspnœa and loss of weight with cachexia usually develop and the cough and expectoration are more marked The latter is often of the typical " currant jelly " or " prune juice appearance due to altered blood Microscopically groups of large fatty cells, or irregular epithelial cells may be seen Malignant cells may be found in 60 per cent of cases by Dudgeon s wet method There are usually no definite physical signs until the tumour causes pressure upon the bronchi, medi astinum or deep thoracic veins or nerves The chest wall may bulge locally, owing to the presence of a growth near the surface or it may be retracted if a main bronchus is obstructed An actual subcutaneous swelling caused by the tumour eroding through the chest wall may be visible Enlarged veins often run across the chest, and one *or other arm may be swollen or œdematous if there is mediastinal obstruction* Vocal fremitus is often unaffected but is increased when the growth is near the surface, and diminished if pleural effusion has occurred The percussion note over a moderate-sized tumour is impaired and may be extremely dull, more often the dullness is due to collapse of the lung The breath sounds vary with the size and position of the growth and with the displacement or pressure effects produced They may be weak, or loud and stridorous The stridor is usually unilateral Adventitious sounds depend upon the presence of complications such as bronchitis Some degree of fever often occurs The supra clavicular and axillary glands are not infrequently enlarged and evidence of malignant disease may be present in other parts of the body such as the abdomen

One special variety of apical carcinoma is the superior pulmonary sulcus or Pan coast tumour, which gives rise to a somewhat characteristic or suggestive clinical picture The chief symptoms are pain in the shoulder inner side of the arm and fore arm together with weakness and wasting of the small muscles of the hand Paralysis of the cervical sympathetic on the same side develops There is usually localised dullness at the extreme apex Radiological investigation reveals a sharply defined apical shadow with destruction of the posterior part of the first three ribs and some times localised vertebral erosion Pancoast suggested that these tumours may arise from remnants of the fifth branchial cleft

Complications and Sequelæ —*Bronchitis is nearly* always present in some degree Pulmonary collapse fibrosis bronchiectasis emphysema, gangrene hæmop tysis pleural effusion abscess and empyema are sometimes observed The effusion is frequently bloodstained In cases of primary malignant disease of the lungs *secondary deposits may occur in other parts of the body such as glands* brain supra renals, heart and bones Cardiac arrhythmia such as auricular fibrillation may result from direct invasion of the pericardium or myocardium

Carcinoma of the lung may be accompanied by neurological syndromes which are not due to secondary deposits and which may cause symptoms before the car cinoma Four types of neuropathy are recognised subacute cerebellar degeneration sensory neuropathy polyneuritis and motor neuropathy The clinical manifestations are not always clear cut and there may be evidence of multiple lesions in the nervous system The characteristic picture of subacute cerebellar degeneration is of a rapidly progressive ataxia and dysarthria diplopia euphoria and dementia are common and there may be *pyramidal and sensory changes In sensory neuropathy* the pre senting symptoms are pain and paræsthesiæ in the limbs and ataxia there is peri *pheral sensory impairment and ataxia*, absent tendon reflexes and only slight muscular weakness In polyneuritis there are motor and sensory changes In motor neuro

pathy there is a progressive atrophic paresis predominantly affecting the limb girdles, bulbar palsy diplopia and ptosis may occur, the tendon jerks are diminished or absent there are often subjective sensory manifestations such as pain cramps or paræsthesiæ but objective sensory changes are rare

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Symptoms —Simple tumours except adenomata are pathological curiosities, and as a rule only produce symptoms when they cause obstruction of a bronchus or press on mediastinal structures (see pp 972 1094)

The early symptoms of malignant growths are slight, and consist of malaise with, perhaps, cough and expectoration Later when the growth becomes more extensive and exerts pressure on, or involves the larger bronchi, mediastinum or pleura, they are more noticeable Pain dyspnœa and loss of weight with cachexia usually develop and the cough and expectoration are more marked The latter is often of the typical "currant jelly" or "prune juice" appearance due to altered blood Microscopically groups of large fatty cells or irregular epithelial cells may be seen Malignant cells may be found in 60 per cent of cases by Dudgeon s wet method There are usually no definite physical signs until the tumour causes pressure upon the bronchi medi astinum or deep thoracic veins or nerves The chest-wall may bulge locally owing to the presence of a growth near the surface or it may be retracted if a main bronchus is obstructed An actual subcutaneous swelling caused by the tumour eroding through the chest wall may be visible Enlarged veins often run across the chest, and one or other arm may be swollen or œdematous if there is mediastinal obstruction Vocal fremitus is often unaffected, but is increased when the growth is near the surface, and diminished if pleural effusion has occurred The percussion note over a moderate sized tumour is impaired and may be extremely dull, more often the dullness is due to collapse of the lung The breath sounds vary with the size and position of the growth and with the displacement or pressure effects produced They may be weak or loud and stridorous The stridor is usually unilateral Adventitious sounds depend upon the presence of complications such as bronchitis Some degree of fever often occurs The supra clavicular and axillary glands are not infrequently enlarged and evidence of malignant disease may be present in other parts of the body such as the abdomen

One special variety of apical carcinoma is the superior pulmonary sulcus or Pan coast tumour which gives rise to a somewhat characteristic or suggestive clinical picture The chief symptoms are pain in the shoulder, inner side of the arm and fore-arm together with weakness and wasting of the small muscles of the hand Paralysis of the cervical sympathetic on the same side develops There is usually localised dullness at the extreme apex Radiological investigation reveals a harply defined apical shadow with destruction of the posterior part of the first three ribs and some times localised vertebral erosion Pancoast suggested that these tumours may arise from remnants of the fifth branchial cleft

Complications and Sequelæ —Bronchitis is nearly always present in some degree Pulmonary collapse fibrosis bronchiectasis emphysema gangrene hæmoptysis pleural effusion abscess and empyema are sometimes observed The effusion is frequently bloodstained In cases of primary malignant disease of the lungs secondary deposits may occur in other parts of the body such as glands brain supra renals heart and bones Cardiac arrhythmia such as auricular fibrillation, may result from direct invasion of the pericardium or myocardium

Carcinoma of the lung may be accompanied by neurological syndromes which are not due to secondary deposits and which may cause symptoms before the car cinoma Four types of neuropathy are recognised subacute cerebellar degeneration sensory neuropathy, polyneuritis and motor neuropathy The clinical manifestations are not always clear cut and there may be evidence of multiple lesions in the nervous system The characteristic picture of subacute cerebellar degeneration is of a rapidly progressive ataxia and dysarthria diplopia, euphoria and dementia are common and there may be pyramidal and sensory changes In sensory neuropathy the pre senting symptoms are pain and paræsthesiæ in the limbs and ataxia there is peri pheral sensory impairment and ataxia, absent tendon reflexes and only slight muscular weakness In polyneuritis there are motor and sensory changes In motor neuro-

pathy there is a progressive atrophic paresis predominantly affecting the limb girdles, bulbar palsy diplopia and ptosis may occur the tendon jerks are diminished or absent there are often subjective sensory manifestations such as pain cramps or paræsthesiæ but objective sensory changes are rare

Diagnosis—This is difficult in early cases and not easy in some advanced ones It not infrequently happens that metastases especially in brain or bone afford the earliest manifestations to be recognised Difficulties may arise in connection with pulmonary tuberculosis fibrosis and gumma of lung aneurysm pericardial and pleural effusion and enlargement of the mediastinal glands due to Hodgkin s disease or tuberculosis The whole body should be searched for evidence of malignant disease elsewhere The sputum should be examined repeatedly for tubercle bacilli and for cellular elements and a radiographic examination made of the chest Localised pulmonary collapse thus demonstrated may be a very early indication By the stereoscopic method excellent evidence of pulmonary neoplasms is often obtainable Lipiodol injection and radiographic examination or tomography may demonstrate the obstruction of a bronchus by the growth which often presents a tapering or rat tail appearance Bronchoscopy is essential in the diagnosis of bronchial carcinoma Temporary artificial pneumothorax may be helpful in diagnosis particularly in differentiating simple tumours in the periphery of the lung growths in the mediastinum and in the chest wall

The Pancoast tumour may give rise to special difficulty It has to be differentiated from syringomyelia cervical rib apical pulmonary tuberculosis and secondary sarcoma

Course—This is progressive the patient gradually losing strength and dying from cachexia or some intercurrent affection

Prognosis—Apart from those cases in which early recognition may in suitable conditions render lobectomy or pneumonectomy with removal of the growth possible this is hopeless death occurring in a few weeks or being delayed for 2 or 3 years The possibility of a successful pneumonectomy is more favourable with differentiated than with undifferentiated types of growth In the latter the growth tends to be more infiltrating and the glands are more likely to be involved

Treatment—Benign tumours are often capable of complete removal with gratifying success

In malignant growths lobectomy or dissection pneumonectomy with complete removal of the growth is only practicable for cases recognised early in which there are no secondary deposits

Radiotherapy may be useful by diminishing local pressure and relieving symptoms but cure by this method is rare

Useless cough should be checked by sedative lozenges or a linctus Dyspnœa due to pleural effusion may be relieved by tapping with or without air replacement but the fluid often reaccumulates rapidly Pain should be relieved by analgesic drugs and in the later stages those containing opium or its alkaloids may be required

TROPICAL DISEASES OF THE LUNG

Paragonimiasis or Distomatosis—Paragonimiasis is a disease contracted in parts of Korea Japan Formosa or China by bathing in or drinking infected water or eating raw crabs or crayfish The symptoms of cough hæmoptysis and pleurisy are caused by the invasion of the lung by flukes

Pulmonary Schistosomiasis—This disease is found in North and South Africa and particularly in Egypt It also occurs in South America and the West Indies It is caused by the invasion of the lung by the ova of *S hæmatobium* or *S mansoni* The ova form tubercles and there is an obliterating endarteritis of the arteriol s

These eventually cause pulmonary hypertension, angiomata and pulmonary artery dilatation

Pulmonary Amœbiasis —Invasion of the lung by *Entamœba histolytica* is usually by direct spread from a hepatic abscess although primary amœbic abscesses presumably embolic, have been described Invasion is usually accompanied by effusion or empyema The sputum coughed up from the abscess is described as being like anchovy paste and this is an apt description although similar sputum sometimes occurs in pulmonary abscess not of amœbic origin

Amœbiasis is a disease of world wide distribution It is not strictly a tropical disease but it only assumes serious proportions where sanitation is defective or human excrement is used in agriculture

Emetine is usually effective in this condition combined with penicillin or other antibiotics

CYSTIC DISEASE OF THE LUNG

Ætiology —Cysts may be congenital or acquired

(i) *Congenital cysts* are lined with respiratory epithelium and have a wall in which elements of the bronchial wall are present They do not always possess any obvious connection with a patent bronchus and are often associated with congenital abnormalities of the heart or skeleton or with cystic disease in other organs The following varieties are described (*a*) The solitary cyst This may occasionally be inflated to balloon like size and be mistaken for a pneumothorax (*b*) Multiple cysts giving rise to either a soap bubble or honeycomb appearance of a lobe or lobes The cysts usually contain air but may contain clear mucinous fluid or they may become full of pus if they are secondarily infected

(ii) *Acquired Cystic Disease* —Some doubt has been expressed as to whether cystic bronchiectasis is an acquired condition or represents infection of a congenital cystic condition of the lung It is however probable that cystic bronchiectasis is the result of bronchiectasis acquired in early life Cystic bronchiectasis has a characteristic multilocular radiological appearance usually in a lower lobe Operative removal is advisable to prevent complications although this type of bronchiectasis often has a relatively benign course In staphylococcal pneumonia thin walled abscesses or cysts often appear and usually disappear by reabsorption Occasionally the cysts remain and may give rise to no symptoms although they are sometimes associated with bronchiectasis They are probably caused by local alveolar distension due to the check valve action of a partly occluded bronchus The 'ring shadows of tuberculosis are of a similar nature and cysts and cavities similar in character occasionally occur in asthmatics

Symptoms —These vary with the variety of cyst present The large balloon cyst met with in infants or young children may result in severe respiratory and cardiac distress In such cases there is cyanosis dyspnœa and displacement of the trachea mediastinum and heart to the opposite side of the chest The percussion note over the cyst is hyper resonant and the breath sounds are absent Solitary cysts often give rise to no symptoms and are only discovered on routine radiographic examination When infected the clinical features may resemble those of lung abscess or bronchiectasis With multiple medium sized or small cysts no symptoms usually appear until infection occurs though hæmoptysis may occur early When infected toxæmic symptoms develop such as loss of weight irregular fever cough and expectoration which is sometimes offensive Clubbing of the fingers may then soon be noted On examination scattered areas of slight dullness and weak air entry with a few persistent râles may be detected

Course, Complications and Sequelæ —The onset of complications usually

leads to the development of symptoms which call for investigation Thus spon taneous pneumothorax may result from rupture of a cyst In other cases suppuration occurs in the cyst with the formation of lung abscess bronchiectasis or empyema Cerebral abscess may be a late sequel

Diagnosis —This is suggested by radiography and by lipiodol examinations and possibly tomography If the space in the cyst is free from fluid the radiographic appearances must be differentiated from those of pneumothorax an emphysematous bulla a thin walled tuberculous cavity or in some cases a diaphragmatic hernia If the cyst contains fluid further investigations are required to exclude the presence of such conditions as lung abscess encysted pleural effusion or empyema hydatid cyst dermoid cyst or a blood cyst A definite diagnosis can sometimes only be made after operation by microscopical examination of a portion of the cyst

Prognosis.—This varies with the type of cyst present the development of com plications and the treatment adopted In many cases the prognosis is good apart from rupture or infection In the large balloon cyst there is risk of sudden death during an attack of distension

Treatment —The large balloon cysts which are causing respiratory and cardiac embarrassment call for immediate treatment by the insertion of a needle Subse quently the only hope of recovery lies in pneumonectomy

When the cysts are infected, treatment by postural drainage should first be adopted Failure usually follows attempts at surgical drainage or collapse opera tions If the cysts are unilateral and infected the only hope of cure lies in radical removal of the portion of lung involved either by segmental resection lobectomy or pneumonectomy and so in bilateral cases it necessarily follows that no radical cure is possible

SARCOIDOSIS OF THE LUNG

Sarcoidosis is really a generalised disease but it occurs often enough in the lungs to merit a separate description

There are two main pulmonary forms One in which the glands are predominantly involved and one in which there is generalised pulmonary infiltration There is however no hard and fast division between the two conditions The enlarged hilar glands are the commonest form and have been found to be common as a result of mass radiography They usually cause no symptoms at all but they may be associated with other lesions in the bones the eyes or the skin Sometimes the discovery is made as the result of a chest radiograph suggested by the appearance of erythema nodosum The differential diagnosis is from the adenitis of primary tuberculosis lymphosarcoma and Hodgkin s disease and other conditions causing mediastinal glandular enlargement

The glands of sarcoidosis are usually discrete from each other well demarcated and bilateral They may persist for months but their disappearance can often be measured in weeks The Mantoux test is usually negative The generalised pul- monary form sometimes follows the glandular form but if it always does the glandular enlargement stage is often missed The infiltration has the radiological appearance of miliary tuberculosis pneumoconiosis or carcinomatosis The nodules may be as small as the nodules of miliary tuberculosis but are sometimes larger and coarser The hilar glands are often enlarged but not necessarily so The commonest physical signs are similar to those of miliary tuberculosis namely generalised crepitations or fine râles

Symptoms —There are often no symptoms at all in either form and the absence of symptom is often strikingly at variance with the extensive radiological findings Shortness of breath and slight cough are sometimes complained of

Course—The enlarged hilar glands often disappear in a few weeks or months Sometimes the glands remain visibly enlarged after the main enlargement has dis appeared *The miliary type of lesion* may disappear completely with the passage of months but more frequently some striated opacity suggestive of fibrosis remains in some areas Occasionally diffuse generalised fibrosis leading to cor pulmonale is described as a late result of miliary sarcoidosis While cases of diffuse pulmonary fibrosis have been described as cases of sarcoidosis there is often no pathological evidence at post mortem of any sarcoid changes

Cavitation has occasionally been observed in cases diagnosed as sarcoidosis Naturally such an event suggests a diagnosis of tuberculosis but cavitation probably occurs occasionally without tuberculous involvement Some cases of sarcoidosis eventually develop pulmonary tuberculosis but this is not evidence that sarcoidosis is a form of tuberculosis any more than is, for example pneumoconiosis which is often complicated by tuberculosis *The course of sarcoidosis is usually benign*

Diagnosis—This is almost entirely radiological and therefore open to errors of interpretation Occasionally the presence of enlarged groups of glands or the co-existence of other sarcoid lesion confirms the prescriptive diagnosis In the majority of cases the Mantoux test is negative

Treatment—Most cases recover during or in spite of treatment Streptomycin may be worth trying Calciferol in large doses is sometimes given and cases have recovered during either of these treatments Corticotrophin and cortisone are reported to produce symptomatic relief with or without streptomycin but are not usually necessary

HYDATID DISEASE OF THE LUNG

Hydatid cysts may develop in the lung in patients infected by the ova of the *Tænia echinococcus*

Ætiology—Man is the intermediate host of this parasite, and becomes infected directly or indirectly from the dog The modes of infection and the life history of the parasite are elsewhere considered (p 324) Males are more often affected and the condition is commoner amongst agricultural labourers especially amongst shepherds and dog handlers *In Great Britain it is occasionally found in Wales* It is common in the more primitive rural districts of the continent and especially in Argentina Australia New Zealand and the Middle East

Pathology—Hydatid cysts have been described in the lungs in from 5 6 to 16 8 per cent *of cases of hydatid disease in different parts of the world* The right lung is more often the site of the disease than the left, and the cyst is usually basic though it may occur in the upper parts of the lung It is generally supposed that infection of the lung is usually secondary to the liver the ova reaching the lung through the diaphragm but the occurrence of primary lung hydatid suggests the possibility of the embryo gaining access to the general blood stream and thus reaching the lung by the pulmonary artery There is as a rule, a single cyst in the lung but multiple or multilocular cysts are occasionally observed The cyst may become as large as a cricket ball but usually ruptures before it reaches this size *It has the same structure* as hydatid cysts of other organs with ectocyst and endocyst It may develop brood capsules and daughter cysts but is often sterile in this situation

The reactive changes in the lungs are at first irritative and congestive but eventu ally some fibroid changes occur producing a more or less *definite fibroid* capsule around the ectocyst The overlying pleura may become inflamed thickened and adherent when the cyst grows near the surface Rupture may occur into a bronchus into the pleura pericardium or peritoneum or occasionally into the aorta or pul monary vein Rarely the contents of a small cyst may *become inspissated* thus producing spontaneous cure

Symptoms—Until the cyst becomes large enough to cause irritation there may be no symptoms but sooner or later cough and expectoration develop The latter is generally mucoid and frequently bloodstained Dyspnœa becomes apparent and pain results if the pleura is involved The signs may be diminished vocal fremitus localised dullness and weak or absent breath sounds and voice sounds over a limited area generally in the lower lobe A few râles may be audible round the dull area Occasionally with a large cyst there may be some bulging on the affected side, and hydatid fremitus has been described The heart may be displaced in rare cases Radiographic examination generally shows a suggestive rounded shadow with very little change in the surrounding lung except in chronic cases where some fibrosis may be observed

Some degree of eosinophilia is common but not invariable. When rupture into a bronchus occurs there is usually sudden copious expectoration of watery fluid containing hooklets Daughter cysts and parts of the ectocyst may be coughed up and lead to dyspnœa and even suffocation from laryngeal obstruction

After rupture spontaneous cure may result if the ectocyst is expectorated More commonly the cavity becomes infected and the symptoms and signs become those of chronic abscess (see pp 324 1002) Rupture into the pleural cavity produces great pain dyspnœa cyanosis and shock similar to the condition induced by pneumothorax Rupture into the pericardium or into a vein is usually quickly fatal When rupture occurs into a serous cavity urticaria and severe toxic symptoms sometimes develop

Diagnosis—The clinical features of pulmonary hydatid may be suggestive of pulmonary tuberculosis pleural effusion or new growth Diagnosis may be difficult before rupture occurs after this the discovery of hydatid hooklets or pieces of cyst wall may establish the diagnosis In suspicious cases the radiographic findings may be of great assistance and confirmatory evidence may be obtained from cytological and serological examination The former frequently shows eosinophilia and the latter gives complement deviation when a suitable antigen such as extract of hydatid cyst wall is used A precipitin reaction may also be obtained with the fluid from another cyst The Casoni intradermal test with the appropriate antigen has established itself as having special diagnostic value

Course—This is generally progressive though occasionally spontaneous cure occurs either before or after rupture More commonly the cyst causes increasing pressure or irritative symptoms and eventually rupture or suppuration produces acute manifestations

Prognosis—The prognosis is serious owing to the risks of rupture and suppuration Spontaneous cure is rare but can occur After rupture into a bronchus recovery may ensue but more commonly abscess formation results Rupture into a serous cavity is frequently fatal Early surgical treatment either before or after rupture improves the outlook

Treatment—Aspiration of the cyst, either exploratory or therapeutic is to be avoided If the cyst can be diagnosed or localised before rupture the lung should be exposed by thoracotomy the pleura stitched together and the cyst incised the endocyst removed and the cavity drained Suppuration of a pulmonary hydatid must be treated as a pulmonary abscess Removal of a lobe containing a single cyst may be the operation of choice

THE PNEUMONIAS

The ideal classification of the pneumonias would be an ætiological one and the old morbid anatomical distinction between lobar pneumonia on the one hand and lobular or broncho pneumonia, on the other would be even less important than it

has already been made by modern therapy Scadding has devised a classification which ignores rigid morbid anatomical divisions and divides pneumonias into two main groups

(1) The acute specific pneumonias whose ætiology is more or less known, and
(2) The aspiration pneumonias which include most of what used to be called broncho pneumonias

By using the term aspiration pneumonia' he wished to indicate that the inflammatory changes were due to the aspiration of infected secretion, where there has been a breakdown in normal defensive mechanisms Most of the broncho pneumonias follow atelectasis produced by aspiration and the term aspiration therefore, has ætiological significance It is unlikely, however, to replace the well established term broncho pneumonia which suggests very well pneumonia following bronchial infection No exact classification can be made without certainty about ætiology and the distinction between various anatomical types is often impossible and unnecessary as they merge into each other In the descriptions which follow, no hard and fast classification has been attempted but the anatomical division into lobar pneumonias and broncho pneumonias will be referred to since it has sometimes diagnostic significance

LOBAR PNEUMONIA

This term has become almost synonymous with pneumococcal pneumonia and this condition will be described first although as will appear, other pneumonias assume approximately lobar form

PNEUMOCOCCAL PNEUMONIA

Ætiology —*Predisposing causes* —Pneumonia may occur at any age It is common in children up to the sixth year the incidence being about equal in the two sexes It is commonest between the ages of 15 and 40 when there is a preponderance in the male sex of 2 or 3 to 1 It is also a frequent terminal malady in the aged of both sexes It may be doubted whether race has much influence although in America and in the Rand mines and throughout Africa the incidence and mortality among the black races are both high Pneumonia is met with all over the world In this country its seasonal incidence is well marked it is uncommon in the summer and autumn and is most prevalent from November to March Although pneumonia is as a rule endemic and sporadic in its incidence it is generally admitted that localised epidemics occur Urban conditions defective sanitation overcrowding and insufficient ventilation all conduce to the incidence of pneumonia It is not uncommon to obtain a history of several previous attacks Although the disease often attacks those in normal robust health there can be no doubt that debilitating conditions and diseases predispose to it among them being chronic nephritis, diabetes over fatigue exposure and alcoholic excess

Exciting causes —The exciting cause in most cases is the presence of the pneumococcus (*Str pneumoniæ*) It may be the only pathogenic organism found in the lung lesions and in the sputum but not infrequently others such as streptococci, staphylococci or *H influenzæ* are also present

The pneumococcus —The pathogenicity of the pneumococcus has been the subject of an interesting study by Cole Dochez Avery and Gillespie and more recently by Georgina Cooper and her co workers Originally three types were described Types I II III which together account for more than 50 per cent of all cases The remainder were included in a group referred to as Group IV This has now been separated into 29 other types making 32 in all by means of serological reactions

The American observers have shown that 40 per cent of contacts with cases of pneumonia due to types I and II may harbour the corresponding organism for an average of 23 days and that they may develop pneumonia from it They have further demonstrated that a convalescent patient may carry pathogenic pneumococci in his mouth for as long as 90 days from the onset of the disease They have also found pathogenic pneumococci in the dust of rooms in which patients suffering from pneumonia have been nursed The significance of this work is obvious It confirms the view that pneumonia is an infectious disease capable of being spread by carriers by the convalescent patient and by the dust of rooms

Although the pneumococcus is the specific exciting cause its activities are often determined by some other factor such as chill exposure over exertion or injury The presumption is that these conditions lower the general resistance of the individual and thus impair the defensive mechanisms Post operative pneumonia may be a further instance of this but doubtless some supposed cases are in reality due to lobar collapse

Pathology—The pneumococcus is found in the pulmonary lesions and elsewhere when complications occur In some patients it is found in the blood These are referred to as bacteriæmic cases and are usually more severe and often associated with complications Experimental investigations on animals indicate that the avenue of infection to the lungs is by way of the trachea and bronchi the blood infection being secondary to the pulmonary lesion Four stages are commonly described in the process by which the lung becomes consolidated and returns to normal namely engorgement red hepatisation grey hepatisation and resolution

In the stage of engorgement the affected part of the lung is slightly enlarged deep red in colour and heavier than normal although it still crepitates and floats in water The pleura over it may be injected and lustreless and may even show early fibrinous exudate On section the hyperæmia is obvious and there may be some œdema On squeezing frothy bloodstained fluid exudes Microscopically the engorgement of the capillaries and the swelling and partial desquamation of the alveolar epithelium are the chief changes to be noted In the stage of red hepatisation the affected area becomes completely consolidated the general aspect on section being remotely similar to liver hence the name hepatisation The pleura is now notably inflamed and may be obscured by yellow fibrinous exudate The hepatised area of lung is larger and much heavier than normal and bears the impress of the ribs upon it On section it is seen to be red in colour solid and completely airless It does not crepitate and it sinks in water The lung tissue is found to be more friable than normal On scraping the cut surface which has a granular appearance a reddish fluid is collected containing small fibrinous plugs which are practically alveolar casts Microscopically the alveoli are occupied by a coagulated exudate rich in fibrin and red blood corpuscles with scanty leucocytes and a few larger cells derived from the alveolar epithelium In the stage of grey hepatisation the lung tissue although still solid airless and non crepitant is greyish in colour softer in consistence and still more friable The surface of the section is less granular and on scraping a pale yellowish almost purulent fluid is obtained Microscopically the blood vessels are found to be relatively empty the alveoli are now incompletely filled the fibrin and red corpuscles have largely disappeared and the alveoli are occupied by leucocytes and desquamated alveolar cells In the stage of resolution the exudate becomes more liquid and its cellular constituents undergo fatty degeneration The liquefied exudate is largely absorbed although expectoration may possibly assist in its removal The lung returns to its normal spongy state and the alveolar epithelium is replaced Some pleural thickening or adhesion may however result In very severe and fatal cases the stage of resolution may be replaced by one of purulent infiltration in which the lung becomes paler softer and in places almost diffluent The scrapings are practically purulent

Although these four stages are described it should be remembered that they are

not sharply defined from one another and that they only represent special appear ances in a continuous process Consequently, although the major part of the affected area of lung may be characteristic of any one of them all four stages may be recognis able especially in cases of a spreading type The base is more often affected than other parts, and the right side more than the left, in the ratio of 3 to 2 The unaffected parts of the lung may show some catarrhal bronchitis or some degree of collateral hyperæmia or œdema Pleurisy is an integral part of the affection, but it may proceed to serous or purulent effusion Pericarditis and less frequently acute endocarditis may be found in fatal cases Pneumococcal meningitis, arthritis and otitis are very occasionally observed The liver and kidneys may show cloudy swelling and the spleen is often slightly enlarged and soft Jaundice may be observed especially in right sided cases The right side of the heart may be engorged and dilated

Symptoms —The following description is based on the symptomatology and progress of a patient untreated with antibiotic therapy There was great variation in both even before antibiotic therapy, but this has very much curtailed and altered the course of the disease The exact incubation period is not yet established, but it is short being probably from 1 or 2 days up to a week The onset is sudden and acute, with chill shivering or rigor in the majority of cases In children convulsions take the place of rigors Vomiting at the onset is not infrequent occurring in about one third of the cases Less commonly the onset is insidious, or is preceded by malaise and catarrhal symptoms The temperature rises with the rigor and, as a rule, a short dry irritating cough develops quickly, accompanied by a severe cutting pain on the affected side The pain often becomes intense, and coughing may cause the patient great distress The cough is frequently restrained as much as possible and the breathing is rapid and shallow By the second or third day the pain becomes less and the cough easier and more effective Sputum, which at first is scanty, extremely viscid tenacious and difficult to expectorate, now becomes more abundant, although remaining viscid In typical cases it is characteristically rusty at this stage containing mucus altered red blood corpuscles alveolar epithelium and large numbers of pneumo cocci In a few instances a small but definite hæmoptysis occurs Occasionally the sputum is thinner and of ' prune juice type

Sleeplessness is often a distressing symptom especially in the early and late stages In some cases there are marked cerebral symptoms Headache at the onset is common Delirium is frequent particularly in the asthenic type in apical cases and in alcoholics In the latter it may be violent and is often like delirium tremens The temperature is usually of high continuous type throughout, reaching 103 , 104° and even 105° F or more on occasions Defervescence is by crisis in about 60 per cent of the cases The most common day for the crisis is the seventh It is rare before the third or after the ninth day At the crisis the temperature falls to normal or subnormal in about 12 hours The patient often sleeps soundly at this time and may sweat profusely respiration is slower and easier and the pulse rate falls On waking a dramatic change in the condition is usually noticeable Pain and distress are ameliorated cough is loose and easy and the patient feels better, although weak Looseness of the bowels and free diuresis are not infrequent constituting the critical evacuations ' The crisis is sometimes preceded by a pseudo crisis in which a considerable fall of temperature occurs with little or no improvement in the general condition A slight post critical rise of temperature of 1 or 2° F is sometimes seen but as a rule the temperature remains subnormal for a few days and slowly returns to normal The pulse rate may be slow for a time Convalescence is generally rapid although in cases which have had marked delirium some mental confusion may be present for a day or two Defervescence by lysis is more common in asthenic patients The temperature remits and may take from 2 to 4 days to reach normal or subnormal levels

The physical signs vary with the stage of the disease At first there is some

restlessness but soon the patient assumes a dorsal decubitus or lies more on the affected side The cheeks are flushed often markedly so on the side of the lesion The eyes are bright but the expression is one of pain or anxiety A crop of herpes *on the lips is very common* The *tongue is thickly coated and white, becoming dry* and cracked in bad cases at a later stage The skin feels dry and pungently hot The alæ nasi are in action and in children a puff or grunt accompanies each expiration while the pause follows inspiration, instead of expiration The respiration and pulse rate are increased the former disproportionately so that the pulse respiration ratio becomes 3 or even 2 to 1, instead of the normal 4 or 5 to 1

In the early stage the pulmonary signs are slight At the most there is lessened movement and diminished vocal fremitus over the affected area with dubious impairment of note, weak air entry and possibly a few crepitations (indux) or pleural friction sounds vocal resonance being unaltered Of these lessened air entry is probably the most common Slight hyper resonance of the opposite lung with harsh breathing may lead to error in diagnosis as to the side affected

The signs of consolidation (hepatisation) are generally apparent on the second or third day except in cases where the disease starts deeply (central pneumonia) There is definite limitation of movement on the affected side which is however slightly increased in size as can be demonstrated by mensuration Vocal fremitus is markedly accentuated over the affected area except in massive pneumonia and friction fremitus may be palpable The note on percussion is dull, but has not the resistant stony character of that over an effusion The note above or below the consolidated area is sometimes skodaic The breath sounds are tubular, and a few crepitations may be heard but frequently adventitious sounds are absent In some cases a friction rub is audible Bronchophony and pectoriloquy are usually very marked over the consolidated area Whispering pectoriloquy usually corresponds exactly to *the area of bronchial breathing and often draws attention to it* The breath sounds in other parts may be vesicular or harsh and a few rhonchi may be present The heart is usually in its normal situation but is sometimes slightly displaced away from the affected side In later stages the signs of dilatation of the right heart may become apparent

During resolution which begins after the crisis or during lysis the tubular character of the breath sounds disappears Coarse moist sounds known as redux crepitations are heard both with inspiration and with expiration The dullness gradually diminishes and the voice sounds return to normal

In basal cases in which the diaphragmatic pleura is involved early there may be pain tenderness and abdominal rigidity simulating peritonitis perforation or appendicitis It is rare for the spleen to be sufficiently enlarged to be palpable The blood shows a leucocytosis up to 20 000 occasionally up to 50 000 in young patients A low white count in a very ill patient is an ominous sign Blood culture may yield pneumococci although this was successful in only 30 per cent of cases at the Rockefeller Institute The urine is diminished in quantity and there is a great reduction in the sodium chloride excretion until the crisis Albumin and albumose are frequently found in small quantities in the urine during the febrile stage and a few granular casts may be present The uric acid excretion is increased to two or three times the normal commencing the day before the crisis and generally falling to normal during the ensuing week This is probably due to disintegration of the exudate in the alveoli and so forms a measure of resolution although some authorities maintain that it runs parallel with leucocytosis and not with cell destruction Pneumococci can sometimes be obtained from the urine at the height of the disease

The stages of the disease are very considerably modified by the early administration of penicillin and to a less extent by the use of sulphonamides Thus if the penicillin injections are begun on the first day of the disease, when the physical signs are slight the temperature will often fall to normal within 24 to 48 hours, with a

corresponding reduction in the pulse and respiration rates The general condition of the patient also rapidly improves pain disappears and toxic symptoms are abolished On the second or third day however the physical signs of consolidation may be well marked, despite the absence of all signs of toxicity

The disease does not always follow the typical clinical course and certain varieties are described

Apical pneumonia —The consolidation may be limited to the apex or upper lobe of one lung This is more common in children, the aged and alcoholics and is often associated with marked cerebral symptoms

Creeping pneumonia (Migratory or wandering pneumonia) —The consolidation spreads irregularly in one or both lungs Partial resolution occurs but there is no true crisis, and as successive portions of the lungs become involved the temperature exacerbates, eventually falling by lysis in cases that recover

Central pneumonia —The symptoms and appearance of the patient may suggest lobar pneumonia, and yet no abnormal signs can be detected in the lungs In some of these cases there may be a deep seated consolidation which can usually be revealed by radiography A typical crisis may occur

Massive pneumonia —The bronchi as well as the alveoli may be filled with a fibrinous exudate It is a rare condition and leads to difficulty in diagnosis as the physical signs resemble those of pleurisy with effusion vocal fremitus being diminished and breath sounds weak or absent The heart however, is not displaced or only slightly so

Post operative pneumonia —It is probable that some cases that were formerly described as post operative pneumonia were in reality instances of massive lobar collapse (see p 992) At times a pneumococcal pneumonia follows the administration of a general anæsthetic but it does not present any peculiar features

Traumatic pneumonia —The fact that an injury to the chest may be followed after a short interval by a pneumonic process in the lungs has long been recognised The condition was called contusional pneumonia by Litten in 1881 Kulbs showed later that the changes in the lungs in dogs following local trauma were mainly hæmorrhagic and that the lung opposite to the side injured may be affected by contre coup In the recorded cases of traumatic pneumonia two types can be differentiated —(1) those with hæmorrhagic lesions only and (2) those showing hæmorrhagic foci with a superimposed bacterial infection The former recover rapidly the latter often lead to a fatal issue Both these types are found in blast injury to the lung produced by close proximity to explosions in air or in water

Pneumonia in children —This often presents certain characteristic features There is rarely any sputum, the expectoration being swallowed Convulsions at the onset are common The lesion is often at the apex of the lung Cerebral symptoms are frequent and empyema or otitis media often occurs as a complication

Pneumonia in the aged —This occurs frequently as a terminal infection often leading to a rapid and comparatively painless death The onset may be insidious and the physical signs slight

In *pneumonia in the insane* lobar consolidation is often observed without marked constitutional disturbance other than fever

Secondary pneumonia —Lobar pneumonia may develop during the course of certain acute specific fevers notably enteric typhus and plague It is doubtful whether a true lobar pneumonia occurs in influenza the condition to which the name influenzal pneumonia is applied being due to coalescing lobar pneumonia with hæmorrhagic extravasations

Complications —Delayed resolution not infrequently occurs the signs of consolidation persisting for weeks instead of days Frequent careful examinations should be made and possible errors in diagnosis considered such as the presence of tuberculosis or empyema Gangrene and abscess are rare but recognised complications

Dry pleurisy is an invariable accompaniment when the consolidation reaches the surface and in a considerable proportion of cases slight serous effusion occurs This occasionally becomes frankly purulent and an empyema results Bronchitis is common and may be due to a complicating secondary infection Cardiac failure is a grave occurrence and can be recognised by increasing cyanosis lividity and dyspnœa with signs of enlargement of the right heart and with enfeeblement of the heart sounds Pericarditis is not very uncommon and is a serious complication It may be dry or proceed to serous or purulent effusion Acute endocarditis sometimes of infective type occurs Abdominal complications are comparatively rare They include pneumococcal peritonitis colitis and nephritis Acute dilatation of the stomach occurs in rare cases and is usually rapidly fatal Meteorism is more common and although serious is more amenable to treatment Jaundice due to hepatitis or to hæmolysis is sometimes present

Pneumococcal meningitis supervenes in rare cases and was invariably fatal before the use of sulphonamides and penicillin Delirium has already been referred to and is especially serious when occurring in alcoholics Peripheral neuritis has been described but is very uncommon Otitis media and arthritis proceeding sometimes to suppuration occur as complications both being commoner in children A parotitis sometimes going on to suppuration is an occasional and serious complication especially in old people During convalescence thrombosis of the veins of the legs may occur in rare instances

Sequelæ of lobar pneumonia are uncommon Perhaps the most remarkable is the liability to subsequent attacks although a history of repeated attacks of pneumonia often suggests a diagnosis of bronchiectasis with recurrent pneumonitis Some permanent pleural thickening or adhesion may occur and after an empyema the usual sequelæ may result Pulmonary fibrosis (chronic interstitial pneumonia) is rare especially in comparison with its frequency after broncho pneumonia this may lead to bronchiectasis

Diagnosis —When the disease is well established and the history is available diagnosis is as a rule easy To prove the pneumococcal origin sputum examination lung puncture or blood culture is necessary

At the onset especially before the signs of consolidation develop difficulties in diagnosis often occur The initial rigor or convulsion with vomiting may suggest scarlet fever In children especially those with early apical pneumonia headache vomiting convulsions head retraction squint and even slight Kernig s sign may lead to an erroneous diagnosis of meningitis Pain in the side and cough the altered pulse respiration ratio and the presence even of slight abnormal physical signs in the chest usually suffice in both instances to suggest the correct explanation

Occasionally the onset of pneumonia may simulate an acute abdominal condition such as appendicitis or perforation of a gastric ulcer owing to referred abdominal pain sometimes with rigidity The diagnosis may be very difficult and laparotomy has not infrequently been carried out in error The history the pulse respiration ratio the absence of tenderness on rectal examination and the presence of pulmonary signs usually enable a correct decision to be made

Influenza may start acutely and simulate pneumonia but the distribution of the signs and the examination of the sputum generally serve to distinguish between them Typhoid fever less often gives rise to difficulty but some cases of pneumonia pass quickly into a typhoid state while some cases of typhoid fever develop consolidation in the first week

When consolidation is well established the chief conditions to be differentiated are—(1) Broncho pneumonia The slower onset the more prolonged course the bilateral patchy physical signs and the marked predominance of the bronchitic manifestations usually suffice to differentiate this group of conditions (2) Secondary pneumonias such as those in plague typhoid fever and influenza can be diagnosed

only from the history the associated symptoms and signs, and from the bacteriological examinations (3) Friedlander's pneumonia is rare Its course is short, its prognosis grave and it can only be recognised by bacteriological investigation (4) Massive collapse The diagnosis of this condition and its differentiation from pneumonia are discussed on p 993 (5) Acute pneumonic tuberculosis The onset and early signs may be identical with those of pneumonia The persistence of the fever its tendency to become remittent or intermittent and the occurrence of night sweats should suggest looking for tubercle bacilli in the sputum (6) Pleural effusion and empyema Differentiation is generally easy, except in cases of massive pneumonia Investigation of the position of the cardiac impulse and of vocal fremitus and resonance, affords the most valuable aid Grocco's triangle may also assist. In some cases the diagnosis can only be established by the exploring needle (7) Infarction of the lung in cardiac disease causing pain cough bloodstained expectoration and dyspnœa may simulate pneumonia The absence of fever the presence of the cardiac condition and the localised physical signs are generally characteristic (8) Acute œdema of the lung especially in mitral stenosis may suggest pneumonia Fever is generally absent the sputum is typical and the primary cause may be apparent. An attack of paroxysmal tachycardia may give rise to difficulty when it leads to dullness and crepitations at the bases but careful examination should establish the very rapid action of the heart and the evidence of venous engorgement in other parts

Course —The course depends on the type and virulence of the infection on the resistance of the patient and the method of treatment employed Since the use of sulphonamides and penicillin in treatment the course is much more favourable and the temperature usually falls to normal or subnormal in 2 or 3 days In fatal cases death commonly occurs between the fourth and tenth days although severe cases may prove fatal as early as the first or second day After the tenth day a fatal result is generally due to complications

Prognosis —Lobar pneumonia is a serious disease The prognosis is profoundly influenced by age and by recent methods of treatment It is infrequently fatal in childhood except in the first years of life After the age of 60 the mortality until the new chemo therapeutic measures were employed was from 60 to 80 per cent The New York investigations at the Rockefeller Institute demonstrated the importance of the type of pneumococcus in prognosis , thus it was found that the mortality of cases with types I and II was about 25 to 30 per cent of those with type III 50 per cent and of other types collectively only 12 per cent The mortality in Great Britain before the use of sulphapyridine about the year 1938 was never as high as in the U S A , being at the outside about 16 to 20 per cent in groups of all ages With the sulphonamides and penicillin the average mortality of all types has been reduced to about 8 per cent

The previous habits and history of the patient influence prognosis considerably chronic alcoholism doubles the risk of a fatal issue and the outlook is grave in patients who are the subjects of diabetes chronic cardio vascular disease nephritis marked debility or obesity Unfavourable indications during the course of the disease are profound toxæmia a pulse rate persistently 130 or more a blood pressure in milli metres of mercury lower than the pulse rate and a temperature remaining at 105 F or over for several days Absence of the usual leucocytosis is generally of sinister import Dilatation of the right heart with cyanosis progressing to lividity is most grave

Of complications meningitis is serious unless it responds to treatment by sul phonamides or penicillin while septic endocarditis is extremely grave Cases with abscess or gangrene although serious sometimes recover especially if operative treat ment is practicable The prognosis of those with pericarditis is serious but not uniformly unfavourable Cases with bilateral empyemata show a high mortality Late delirium is a very serious indication

Treatment —The patient should lie in a narrow bed away from a wall to facilitate

nursing The room should be well ventilated and the temperature maintained at 60° to 65 F Treatment in the open air is not advisable except in very mild weather Two important factors are rest and sleep The patient should therefore be disturbed as little as possible by the examination of the physician and by the attentions of the nurse His position in bed should be dictated by his own preference but most patients prefer to be propped up on two pillows In severe cases where the patient tends to be immobile on his back he must be turned to either side to prevent postural collapse The patient usually has no appetite during the acute stage He should however be encouraged to drink 3 or 4 pints daily of sweetened fluid flavoured with fruit juice Sweetened milk suitably flavoured should be given if liked but too much milk is not well tolerated Soups with a little extra salt help to prevent salt depletion As the temperature falls and appetite returns a digestible but high calorie diet should be encouraged

The irritating cough which is so painful at the outset should be checked by a sedative linctus but it may be necessary to inject gr $\frac{1}{12}$ diamorphine hydrochloride or gr $\frac{1}{6}$ morphine to reduce the pain and induce sleep in the early stage The application of a kaolin poultice or Antiphlogistine is traditional and may afford some relief Severe pain can be controlled by properly applied strapping This has the theoretical disadvantage of diminishing movement and thus encouraging collapse but nothing is more likely to prevent coughing up of sputum from the affected lung than severe pain If strapping is applied it should be removed as soon as possible

The sulphonamide group of drugs is very effective Sulphadimidine is probably the best for an adult and the treatment should be started with an initial dose of 3 g followed by 1 g 4-hourly until the temperature has been normal for 36 hours and then progressively diminished until the treatment stops about 5 days after the fall of the temperature The sputum should be taken for cultivation before treatment starts so that if there is no response to treatment the results of sensitivity will be available to guide any change in therapy

The dosage in children depends on the body weight, but as a rough guide an initial dose of 0 5 g should be given to a child from 0 to 1 year with a maintenance dose of 1 0 to 1 5 g in the 24 hours and from age 1 to 3 1 0 and 2 0 g to 3 0 g as maintenance and so up in proportion

If there is any doubt about the response or the patient is sensitive to sulphonamides or is very ill it is wise to give penicillin instead of or as well as the sulphonamides Particular care must be taken to see that these dehydrated patients have an adequate fluid intake and output during sulphonamide therapy

If there is any cyanosis the patient should be given oxygen preferably in an oxygen tent *The B L B mask unless carefully supervised is often ineffective and in any* case the cough and sputum complicate the use of a mask If a tent is not available the nasal catheter in the naso pharynx is better than the mask in most cases

Digitalis is often given in small doses but is probably of no value Injections of nikethamide (Coramine) are not of proved value but they are sometimes comforting to the patient and the doctor Sleeplessness is a frequent and distressing symptom In the early stages gr 10 of Dover's powder or an injection of gr $\frac{1}{6}$ or $\frac{1}{4}$ morphine are usually effective It is best to avoid morphine if the patient is cyanosed Chloral hydrate gr 20 and potassium bromide gr 20 can be tried or amylobarbitone (Sodium Amytal) gr 3 to 6 Paraldehyde min 120 with syrup of orange in 2 oz of water is safe or it can be given rectally in doses of 4 to 6 drams in 6 oz of water

If there is any tendency to delirium the patient should have tepid sponging and be given any of the sedatives mentioned previously They should not be left unattended as they are liable to get out of bed and fall down stairs or out of windows Tympanites when present is distressing and exhausting and should be treated by the passing of a rectal tube or by giving an enema Pituitary extract (0 5 ml.) or *neostigmine (1 mg) may be tried*

Streptococcal pneumonia—This is often lobular but may be confluent so as to appear lobar It usually follows streptococcal infection in other parts of the body especially the throat or the skin It is sometimes found as a secondary invader in nasal infections of the respiratory tract such as influenza or measles but it occurs as a primary infection of the lung The symptoms are often severe and the patient may appear more ill than in pneumococcal pneumonia Thin purulent effusions (sometimes bilateral) occur at an early stage and require aspiration

General treatment is as for pneumococcal pneumonias Most streptococci respond readily to sulphonamide drugs or penicillin

Staphylococcal pneumonia—Staphylococci are found as secondary invaders in viral pneumonias but they also cause a particular type of pneumonia The infection is usually blood borne but may be bronchogenic It may occur as a complication of a septicæmia or a pyæmia arising from a carbuncle perinephric abscess mastoiditis or some other focal lesion, but sometimes the source is not obvious There is con solidation of varying degree not often conforming to any exact lobar pattern, with a tendency to necrose and form thin walled distension cavities Several areas of the lungs may be successively involved Spontaneous pneumothorax may occur through rupture of the thin walled cavities but it is not always followed by empyema as might be expected and the cavities often disappear spontaneously After recovery the cavities sometimes remain as thin walled cysts Bronchiectasis may be a complication

General treatment is the same as described above but large doses of penicillin and sulphonamides should be given Many cases are resistant to penicillin but respond to the tetracyclines or erythromycin

Friedlander bacillus pneumonia—This organism causes pneumonia with a high mortality, especially in older patients Prostration and cyanosis are often striking and the most seriously ill patients have little pyrexia and often a leucopenia Death often occurs within 48 hours of onset The organisms are not sensitive to penicillin or the sulphonamides but may be to streptomycin chloramphenicol or chlortetracycline

There is a chronic form of lung infection due to this organism which sometimes follows the acute infection but may also occur insidiously The cases are often mis taken for fibrocaseous tuberculosis which they resemble

P pestis pneumonia This infection sometimes assumes a pneumonic form which is particularly lethal and infectious It has been described in epidemics in Manchuria and West Africa

Myco tuberculosis—Pneumonia due to this organism is described elsewhere but although it is now rare in Great Britain it is occasionally mistaken at the outset for pneumococcal pneumonia and it must be remembered as a possibility when a lobar pneumonia does not quickly yield to treatment

PNEUMONIAS OF VIRAL ORIGIN

Influenzal pneumonia—In 1933 Smith Andrews and Laidlaw showed that in fluenza was due to a filtrable virus of which two main strains labelled A and B respec tively have been isolated Influenza a highly contagious disease usually presents with fever marked prostration general aches and inflammatory changes in the respiratory tract Although it is often followed by marked depression it is rarely fatal in otherwise healthy adults but occasionally pandemics occur in which pneu monia occurs and the disease is rapidly and frequently fatal The pneumonia in these cases has been ascribed to secondary invaders amongst them *Hæmophilus influenzæ* streptococci staphylococci etc

Primary atypical pneumonia—Synonym, Virus Pneumonia — This diagnosis prob ably includes a varied group of diseases It was recognised before the war of 1914–1918 but came into prominence during the recent war as a result of the large epidemics which occurred amongst soldiers especially in the Mediterranean theatre

Pathology—Little is known of the post mortem findings as the mortality rate is low about 0 2 per cent Observations which have been made indicate that there is an interstitial broncho pneumonia with associated bronchitis and areas of collapse and emphysema The associated bronchi are filled with muco pus The inter-alveolar septa are infiltrated with monocytes

Symptoms—The incubation period varies from 2 to 21 days or longer The onset is often insidious with cough malaise and muscular pains Coryza may be marked at the onset or there may be pain in the chest with dyspnœa Some cases have been detected by routine radiographic examination of the lungs Generally the temperature rises to 100° to 103° F for about a week but some cases are apyrexial Cough may be very distressing occurring in paroxysms and with severe headache There is usually some mucoid sputum at times blood streaked but never rusty The sputum contains no predominating organisms but mononuclear cells are often present The physical signs in the lungs are rather indefinite One or more areas of slight dullness may be detected frequently at the bases with weak air entry and showers of medium râles heard after cough at the end of inspiration The pulse rate is often lower than would be expected from the pyrexia The white cell count is usually normal or there may be slight leucopenia and the sedimentation rate of the red cells is increased and may remain raised for some weeks or months The Wassermann reaction may be positive for a short time Cold agglutinins (auto hæmoagglutinins) have been found in the blood from the second to the fourth weeks of the illness Severe cases are also described with high irregular fever prostration a racking cough cyanosis and dyspnœa The temperature may remain raised for 2 to 3 weeks There are no typical radiological findings Woolly areas of consolida tion of varying size may be seen often at the bases resembling those seen in chronic disseminated or local pneumonia The hilar shadows are usually enlarged more so than they are in early tuberculous lesions and this may be of diagnostic importance

Complications and Sequelæ—The majority of cases are uncomplicated but a pleural effusion may be expected in about 9 per cent of cases and this may be purulent Rarely there are symptoms of encephalitis or meningism venous throm *bosis in the legs* and polyarthritis

Diagnosis—Some cases have been diagnosed as tuberculosis especially when the soft shadows are seen in the upper lobe The prolonged febrile type with relative low pulse rate and absence of leucocytosis may suggest typhoid fever The presence of eosinophils in the sputum or the blood will help to differentiate Loeffler s syndrome which sometimes resembles atypical pneumonia

Course—Febrile recurrences are not uncommon if the patient is allowed up too soon Usually the patient is able to leave hospital in about a month from the onset In some cases the radiographic shadows take 2 months or longer before they disappear

Prognosis—This is usually very good although recovery may occasionally be slow

Treatment—The patient should be kept in bed for a few days after the tempera ture has returned to normal He should not resume work until the sedimentation rate is normal and the radiographic findings are clear Penicillin and the sulphona mides are useless and the sulphonamides may be harmful Some cases respond well to chlortetracycline or chloramphenicol Steam inhalations usually relieve the cough Severe cyanosis or dyspnœa may be treated by oxygen inhalations

Psittacosis—This disease is transmitted by birds of the parrot family as its name implies but it may be transmitted by other birds such as pigeons or canaries The disease is similar to atypical pneumonia but is more severe and carries a mortality of up to 40 per cent The diagnosis should be remembered where pneumonic symp toms are found in someone who is in close contact with birds kept as pets or pro fessionally

Chloramphenicol and chlortetracycline are often effective

Q fever—This is a rickettsial disease which resembles primary atypical pneumonia from which it can only be distinguished by agglutination reactions Some of the epidemics of atypical pneumonia described in the Mediterranean theatre were of this character

PNEUMOCOCCAL LOBULAR PNEUMONIA

Synonym—Primary Broncho pneumonia

Ætiology—Pneumococcal infection in infants usually has a lobular form instead of a lobar one as in older children or adults Lobular pneumonia is really a more correct name than broncho pneumonia in this case since there is no antecedent bronchial inflammation before the lobular pneumonia It occurs equally in the two sexes and is commoner in the winter and the spring Rickets, malnutrition and debility are predisposing conditions

Pathology—Widely scattered patches of consolidation are found in one or both lungs These may be small and separated by areas of collapse or emphysema Occasionally they are almost confluent and at first sight appear like lobar pneumonia, constituting the pseudo lobar form, but careful observation shows that the distribution is lobular and that zones of incomplete consolidation or of normal lung tissue separate the solid areas If the process reaches the surface some degree of pleurisy is present although this is less than in lobar pneumonia

Microscopically the appearances approximate to those of the lobar form, the alveoli are found to be filled with exudate, in which leucocytes and desquamated epithelial cells are present, together with some fibrin and red blood corpuscles Catarrhal changes are also present in the bronchi

Symptoms—The onset is acute with vomiting and chill or convulsion as in lobar pneumonia but may be more gradual Cough cyanosis and dyspnœa develop rapidly There is no expectoration since infants and young children swallow the sputum Cerebral symptoms simulating meningitis are common The temperature rises quickly to 103 104° F or higher and the range is of the same character as in lobar pneumonia Defervescence by lysis is the rule

The physical signs are variable In cases with widespread consolidation they are very similar to those of lobar pneumonia, with dullness tubular breathing increased voice sounds and crepitations In other cases although the aspect of the infant appears characteristic of pneumonia with rapid breathing cyanosis reversed rhythm of inspiration and expiration sucking in of the lower ribs and dilation of the alæ nasi the signs are more scattered Tubular breathing and increased voice sounds may only be heard in localised patches especially in the lower lobes Crepitations are commonly present and rhonchi may be audible over both lungs

Complications and Sequelæ—These are similar to those of lobar pneumonia

Diagnosis—Pneumococcal lobular pneumonia has to be distinguished from the lobar form to which ætiologically and pathologically it is so closely related The acute onset without previous respiratory symptoms will suggest its primary character while the patchy distribution of the signs generally suffices to establish its lobular distribution The cerebral symptoms at the onset and the early absence of pulmonary signs may give rise to difficulty, as in the first stage of lobar pneumonia

Course—This is usually short the temperature falling in from 3 to 7 days but it may be more prolonged and be suggestive of tuberculosis or some other form of secondary bronchitis

Prognosis—The prognosis is generally unfavourable especially in very young or debilitated infants but has been improved by the use of sulphonamides or penicillin

Treatment.—This is practically identical with that of broncho pneumonia in children

BRONCHO PNEUMONIA

Synonyms —Lobular Pneumonia Aspiration Pneumonia Secondary Broncho pneumonia

In this condition there is inflammation of the bronchi spreading down to and involving the alveoli It is generally a catarrhal process but may go on to septic or suppurative manifestations

Ætiology —A secondary broncho pneumonia may occur at any age but is much more common in early and advanced life It is equal in its incidence in the two sexes It frequently occurs as a complication of measles whooping cough and influenza less commonly in cases of diphtheria scarlet fever and the enteric group A bronchitis starting in the larger tubes may spread downwards to the alveoli Broncho pneumonia may develop during the course of acute gastro enteritis A secondary broncho pneumonia occurs as a terminal infection in many old and debilitated persons and in those with chronic wasting or cachectic diseases and also in chronic cardio vascular conditions chronic renal disease and in many progressive nerve degenerations

Bacteriology —This is as might be expected very varied Streptococci are frequently present especially the hæmolytic variety generally associated with other organisms such as the pneumococcus *H influenzæ* staphylococci and those found in catarrhal conditions of the upper air passages *H pertussis* may be found in cases associated with whooping cough and occasionally *C diphtheriæ* in diphtheritic broncho pneumonia The importance of Friedländer's bacillus was formerly overestimated in this connection

Pathology —When from any of the above mentioned causes an inflammatory process reaches the finer bronchi the alveoli become affected in three different ways Owing to the blocking of the bronchi by secretion or exudate, small areas of collapse of lobular distribution are produced The inflammatory process extends into some or all of these and areas of lobular consolidation result Not infrequently the adjacent groups of alveoli become distended and are thus in a condition of acute emphysema The lungs are normal in size or slightly enlarged The surface presents a somewhat uneven mottled appearance There are small projecting patches of firmer consistence and reddish grey colour due to the consolidated lobules Adjacent areas may be depressed and slaty blue from lobular collapse while the intervening lung tissue is normal or pinkish and emphysematous There may be dimness or slight roughening of the pleura where the consolidated areas reach the surface but serous or purulent effusion is uncommon On section the lung is found to be congested and sometimes œdematous especially at the bases while the bronchi exude pus or muco pus from their cut ends The reddish-grey areas of consolidation are found to vary in size from a pin s head to a hazelnut They are generally more abundant in the lower lobes especially posteriorly The consolidated and collapsed areas both sink in water and do not crepitate There is often some peri bronchitis and the bronchial glands are usually enlarged Microscopically the finer bronchi and the consolidated alveoli are found to be filled with an exudate containing large numbers of leucocytes and desquamated proliferating epithelial cells but in which few red blood corpuscles and little or no fibrin are found

In the very acute condition to which the name capillary bronchitis was formerly applied consolidation may not be apparent but microscopical examination invariably demonstrates the involvement of the alveoli In influenzal broncho pneumonia the pathological changes probably commence as an exudative bronchiolitis associated with capillary hæmorrhages Secondary infections are probably responsible for the consecutive broncho pneumonic process which results in flooding of the alveoli with an exudate containing red cells but little or no fibrin

Symptoms —In the cases ensuing on bronchitis in infants or old people (formerly

called capillary bronchitis) initial symptoms may be slight and simply those of ordinary bronchitis namely *malaise slight fever and cough, with or without expectoration* The implication of the finer tubes and alveoli is usually marked by a rapid rise of temperature, great prostration, quick breathing and an irritating, persistent and often ineffective cough In children, the alæ nasi work, the lower ribs are sucked in and the pneumonic type of breathing develops The patient becomes cyanosed the pulse is rapid, 120 or more, and the respirations 50 or 60 per minute In old people, cyanosis, restlessness and delirium may occur and later the cough becomes less frequent, the patient being drowsy and tending to sink down in the bed whereas previously there was orthopnœa These symptoms are ominous and indicate failure of the respiratory centre

The physical signs are often those of bronchitis harsh or weak inspiration and prolonged expiration, sibilant and sonorous rhonchi and crepitations or crepitant râles, especially at the bases Patches of tubular breathing with increased voice sounds may develop, but are not always present

In other forms of secondary broncho pneumonia similar symptoms and signs develop more insidiously in the course of the primary disease Broncho pneumonia should be suspected when cough expectoration and dyspnœa, together with a remittent type of temperature, develop in the course of an acute specific fever or other severe illness In all forms, anorexia is common, the mouth and tongue become dry, and thirst is complained of The urine presents the usual high coloured concentrated character of febrile conditions It is often diminished in quantity, may contain a small quantity of albumin and not infrequently deposits urates

Complications and Sequelæ—These are relatively infrequent Pleurisy may proceed to effusion, and when this occurs it is often purulent Abscess and gangrene are rare but develop rather more frequently than after lobar pneumonia Other complications such as pericarditis endocarditis, meningitis and nephritis are probably due to blood borne metastasis

The most important sequel is bronchiectasis which sometimes follows this condition although it may not give symptoms for a long time afterwards Pulmonary tuberculosis is frequently described as a sequel especially after measles and may be due to inflammatory changes in the bronchial glands activating a quiescent tuberculous deposit there In many cases of tuberculosis described as following on broncho pneumonia it is more probable that the original lung affection was tuberculous

Diagnosis—The development of pulmonary symptoms and of more or less characteristic physical signs in the course of measles whooping cough or one of the other diseases mentioned above usually renders the diagnosis easy Difficulty may arise in regard to tuberculosis which in one form produces lobular pneumonic lesions with symptoms and signs indistinguishable from other varieties of secondary broncho pneumonia In any case where the fever lasts more than 3 weeks or where the signs show no tendency to resolve or are chiefly apical tuberculosis should be suspected Unfortunately in children sputum is rarely available An attempt is sometimes made to obtain it on gauze held in forceps after exciting cough by touching the fauces The mucus in the fauces may also be examined for tubercle bacilli The diagnosis may however remain doubtful until signs of softening become established

Bronchitis rarely gives rise to difficulty The fever is usually less high and of shorter duration while the physical signs are different, signs of consolidation being entirely absent Hypostatic pneumonia may have to be considered There is usually some obvious cause for this such as cardiac disease and failure or prolonged confinement to bed The temperature is generally lower and the distribution is lobar

Pleural effusion and empyema can generally be differentiated by the alteration of vocal fremitus and the displacement of the cardiac impulse In case of difficulty the exploring syringe enables a distinction to be made

Course—Secondary broncho pneumonia generally has a longer course than either

the primary form or the lobar variety of pneumonia The fever often persists in remittent type for 2 or 3 weeks and sometimes even for 2 or 3 months although in this case tuberculosis should be suspected The decline is almost always by lysis Convalescence is often slow the patient being left thin weak anæmic and debilitated

Prognosis—The prognosis in secondary pneumonia is serious Many deaths occur from this complication in the acute specific fevers particularly with measles and influenza Even the form following on severe bronchitis is frequently fatal especially in old people and in wrongly fed or debilitated infants The development of delirium of a pulse rate over 150 of marked cyanosis and dyspnœa is unfavourable In old people drowsiness sinking down in the bed and cessation of cough are very grave indications

Treatment.—The treatment is very similar to that of lobar pneumonia except that stimulant and expectorant drugs may be necessary from the first In cases due to pneumococcal infection sulphadiazine or one of the other sulphonamides should be employed (see p 22) If streptococci are established as the infecting agent one of the sulphonamide preparations should be given at once Penicillin may be given alone or with the sulphonamide preparation but antibiotic preparations are much less effective than in pneumococcal pneumonias The sputum should be tested as soon as possible in order to determine the sensitivity of the predominant organisms

The patient must be in bed and the position should often be changed so as to prevent hypostatic congestion The room should be well ventilated but without draughts and the temperature kept at 65 F both night and day Oxygen should be given if there is any cyanosis however slight The most effective method of giving it is by oxygen tent. The next most effective is by post nasal catheter The B L B mask is rarely used effectively The diet should be restricted to fluids and semi solids as in pneumonia The dry distressing cough at the onset may be loosened by giving a simple alkaline febrifuge mixture such as liq ammon acetat min 120 pot citrat. gr 10 sod bicarb gr 10 with flavouring agents such as syrup of tolu and chloroform water Later ammon carb and tinct ipecac. may be given, but large doses of expectorants are to be avoided because of their irritant effect on the stomach Opiates should not be administered except as tinct opii camphorata or possibly Dover s powder in the early stages In infants they should not be given at all

When in infants or children the bronchi are becoming blocked by the secretion within them as evidenced by increasing dyspnœa an emetic should be given For this purpose tinct ipecac or ammon carb in emetic doses is the most effective In old people ammon carb may be given in milk in doses of gr 10 two or three times a day Deep breathing at regular intervals should be encouraged

Nikethamide (Coramine) or camphor injections and cardiac tonics are of limited value but sometimes give comfort

INHALATION AND DEGLUTITION BRONCHO PNEUMONIA

Acute broncho pneumonic processes may be caused by the inhalation or aspiration of fluid or solid particles derived from the upper air passages or from other parts of the lung To this form the name of aspiration or inhalation pneumonia is applied When from any cause food particles are drawn into the bronchi and broncho pneumonia results the condition is referred to as deglutition pneumonia The resultant processes are similar and are in effect analogous to those caused by other septic or infected foreign bodies inhaled into the bronchi

Ætiology—These conditions may occur at any age but are more common in adult life They result from septic processes in the mouth naso pharynx larynx or

trachea, and from any morbid state leading to anæsthesia of the pharynx or to difficulty in deglutition They occur in association with ulcerating growths of the mouth, tongue, tonsil, pharynx or larynx and after operations for these conditions or upon the nose and throat, including tracheotomy They occur as a complication of achalasia or œsophageal pouches Aspiration broncho pneumonia may also result from vomiting during or after the administration of an anæsthetic Carcinoma of the œsophagus eroding the trachea may be a cause Diphtheritic or other forms of paralysis coma from any cause, especially cerebral vascular lesions and uræmia may lead to the passage of food particles into the air passages Recent work with opaque substances has shown that aspiration of foreign particles occurs more frequently after dental extractions and other surgical operations than is usually realised Other cerebral lesions such as abscess or tumour and bulbar paralysis can also produce the same condition Infected material may be aspirated from diseased to healthy parts of the lung, as in hæmoptysis, abscess, gangrene and bronchiectasis or after rupture of an empyema into a bronchus

Pathology—Any material reaching the air passages in this manner is certain to be laden with infective micro organisms which may induce bronchitis and broncho-pneumonia Since pyogenic organisms are often present suppuration is frequent and single or multiple abscesses result, or even gangrene If the pleura becomes involved empyema may develop

Symptoms—These are in general similar to those of secondary broncho pneumonia and are superadded to those of the primary condition There is generally high temperature, sometimes with rigors cough and expectoration which is occasionally offensive It may be mixed with food material and with blood The physical signs are those of bronchitis and widespread broncho pneumonia

Complications and Sequelæ—These are somewhat similar to those of other inhaled foreign bodies and comprise abscess gangrene and empyema

Course—The course is often short, owing to the severity of the process and the gravity of the primary cause In the comparatively rare cases that recover, the course may be severe and protracted

Prognosis—From the nature of the primary condition and the intensity of the resulting broncho pneumonia this is usually grave

Treatment—Prophylactic.—The utmost care should be paid to the toilet of the mouth and pharynx in disease of or operations upon these parts In paralysed or unconscious patients it may be necessary to resort to nasal feeding In hæmoptysis or bronchiectasis the patient should lie rather on the affected side

In most instances the general treatment is similar to that of broncho pneumonia Postural drainage should be given

TUBERCULOUS BRONCHO PNEUMONIA

This constitutes one form of pulmonary tuberculosis (see Acute Caseous Tuberculosis p 1019)

PNEUMONITIS

Pneumonitis is a term sometimes used as a general term for inflammatory conditions of the lung It has some convenience in describing the inflammatory changes which are found in direct spread from a suppurative bronchiectasis or in association with a neoplasm of the lung which are neither broncho pneumonia nor lobar

R A Young
G E Beaumont
E R Boland

DISEASES OF THE PLEURA

PLEURISY

Pleurisy or pleuritis is an inflammation of the pleural membrane covering the lung or of its parietal reflexions

An ætiological classification, based on the bacteriological findings would be the most satisfactory one, but is at present impracticable chiefly owing to the difficulty of establishing the bacteria concerned in many cases The classification usually adopted depends upon the effects produced If the process leads only to fibrinous deposit it is described as *dry pleurisy* If in addition much serous fluid is poured out the condition of *pleurisy with effusion* results, while if pus is formed the affection is described as *purulent pleurisy* or *empyema*

It is however important to recognise that although such a classification is convenient from a clinical standpoint the three conditions are in reality only stages or degrees in the pleural response to irritative or noxious agents The form occurring in any given case depends upon the nature of the cause the extent of the infection and the degree of resistance possessed by the individual affected Further pleural inflammations may be primary or secondary to local disease or to blood infection and they may be acute or chronic in course

A ACUTE DRY PLEURISY (ACUTE FIBRINOUS OR PLASTIC PLEURISY)

Ætiology—This affection has been described as primary and secondary It is doubtful if such a condition as primary pleurisy exists and it is wise to regard it as secondary to some pulmonary condition At all events the alleged predisposing effects of exposure to cold and wet probably play no part other than by reducing the general resistance and precipitating pulmonary disease

Dry pleurisy secondary to pulmonary disease—Dry pleurisy is a frequent complication or concomitant of many diseases of the lungs notably of pulmonary tuberculosis in any form It is almost invariably present in lobar pneumonia It occurs in association with pulmonary collapse interstitial pulmonary fibrosis bronchiectasis abscess gangrene infarcts and new growths of the lung Injuries of the chest wall disease of the ribs chronic nephritis septicæmia or pyæmia may all be complicated by acute dry pleurisy

Pathology—The inflamed area is often localised but the process may be wide spread or even involve the whole pleural surface Either the visceral or parietal layer may be first affected but as a rule both become involved There is at first hyperæmia with exudation of serum into the subpleural connective tissue The pleura then appears slightly dull or matt instead of shiny Further exudation leads to the deposit of fibrin on the roughened pleural surfaces in the form of a thin false membrane which often presents a rough or even shaggy appearance This membrane consists of fibrin entangling leucocytes a few red blood corpuscles and desquamated endothelial cells

During the process of resolution localised adhesions commonly form but this is not invariable and a patch of thickening without adhesion may be the ultimate result.

Symptoms—The onset is usually sudden with acute pain in the side often described by the patient as a stitch Occasionally a sense of malaise may precede the development of the pain by a few hours or even days but this is not the rule The pain is aggravated by deep inspiration by coughing or even by movement It is often very severe sometimes agonising and the increase of pain, which sometimes

comes as a result of an involuntary cough on deep inspiration is often described as if a knife was being driven into the chest It makes the patient catch his breath or cry out, and he often claps his hand to his ribs *in an involuntary effort to prevent* the movement of his chest wall Cough is generally an early symptom and it is characteristically short dry ineffective and distressing The temperature is usually raised, but, as a rule only to 100° or 101° F and some cases are practically apyrexial

The decubitus is variable The patient may lie on the affected side, but in some cases this aggravates the pain, and it is more comfortable to lie on the back or slightly turned towards the sound side There is diminished movement on the affected side and breathing may be rapid although not dyspnœic On palpation, vocal fremitus is unaffected, but local tenderness of the skin or muscles is sometimes found and occasionally a friction fremitus may be found although this is likely only in the stage of recovery when the pain has almost disappeared The breath sounds are generally unaltered, but they may be short or jerky in the neighbourhood of the lesion The sign of dry pleurisy is the friction rub The characteristics of these rubs depend on the stage of the inflammation and extent of the area involved The most painful rubs are often nearly inaudible because the patient's respiration is inhibited at the time of contact All that may be heard is a sound like a single localised râle which can only be recognised by its tendency to remain in the same place and to coincide with the *catch in the patient s breath as he feels the pain* At other times the rub sounds like a series of superficial dry crepitations As the friction rub becomes less painful it becomes more like creaking or rubbing leather or like the sound of a foot step on crisp crunchy snow The louder the rub the less the pain as a rule The friction sounds may be quite localised or very widespread and they may not be present with every respiration In the acute stage it is inadvisable to ask the patient to take a deep breath or, worse still to cough in order to produce the sound The voice sounds are not altered

Complications and Sequelæ—Dry pleurisy may proceed to effusion but in most cases results in the formation of pleural adhesions The most common sequel is pulmonary tuberculosis sometimes after an interval of years the explanation being *that the original pleurisy is frequently tuberculous* Aching pain in the side with some dyspnœa may be a temporary sequel of dry pleurisy

Diagnosis—The differentiation of dry pleurisy from the other causes of pain produced in, or referred to the chest wall is not always easy and requires careful observation of the case The distinction is important since an erroneous diagnosis of pleurisy may arouse a suspicion of tuberculosis in subsequent febrile diseases The term pleurodynia has been used to include fibrositis of the intercostal muscles and membranes and intercostal neuralgia The term should be avoided since it has a sound full of pomp, signifying, most often ignorance The terms it comprises are themselves suspect for the same reason

It is wise to treat any chest pain which has the characteristics of pleurisy as being pleurisy until it is proved otherwise It is, however quite true that inflammatory or traumatic changes in intercostal muscles may produce pain on respiration rather similar to the pain of pleurisy Inflammation of the intercostal nerves does also occur, but pain and tenderness tends to follow the distribution of the intercostal nerve or its anterior or posterior branches and sometimes when there is infection of the posterior ganglions it is followed by herpes zoster Other conditions inducing pain referred to the chest wall are tumours or aneurysm pressing on the intercostal nerves malignant disease of the spinal cord or of its membranes and caries of the vertebræ Where the pain lasts more than a few days, and no *friction is heard* these conditions should be borne in mind

Bornholm disease is an epidemic disease which causes acute pain of a pleuritic nature Usually the pain appears to be in the muscles of the chest wall but in some

cases pleural rubs have been described In the absence of an epidemic an isolated diagnosis of Bornholm disease should be made with reserve or it may become as unsatisfactory as the diagnosis of pleurodynia

Occasionally adventitious sounds of extra pleural origin may give rise to some difficulty Contraction of the muscles of the chest may cause a muscular ' susurrus grating sounds may be produced in the shoulder joint or in the fascial planes of the back muscles The origin of these sounds can usually be determined by causing the patient to cease breathing while carrying out movements of the shoulder or back muscles Occasionally true friction sounds may have a cardiac rhythm as well as a respiratory one when the area of pleura involved is near the pericardium It is then referred to as pleuro pericardial friction

Having established the evidence of dry pleurisy a careful search should be made for the primary condition Pulmonary tuberculosis pneumonia bronchiectasis and the other causes mentioned above should be considered and excluded

Course —The temperature and pain may subside in 2 or 3 days and convalescence may be rapid if effusion does not occur Occasionally the pain persists off and on for a few weeks but these cases are usually tuberculous and terminate in effusion

Prognosis —Depends entirely on the primary condition of the lung or the disease of which it is a complication

Treatment —The patient should be kept in bed no matter how mild the attack The diet will depend on the general condition and appetite of the patient The pain can often be relieved by strapping the affected side Strips of adhesive plaster are moulded to the chest wall about 2 in from the vertebræ on the sound side of the chest The patient is asked to breathe out and while in this position the strapping (nicked to make it lie flat) is stretched round the affected side and moulded over the sternum on to the sound side again The application should be from below upward and properly applied one or two strips will often be enough to relieve the pain They should be removed as soon as possible to prevent irritation of the skin If the strapping is ineffective and it is certain that it has been properly applied it should be removed

If the pain is intense an injection of gr $\frac{1}{6}$ or $\frac{1}{4}$ of morphine should be given and a small injection of morphine or heroin is often the best way to start any treatment since the patient is often tired and terrified Local applications to the chest such as capsicum ointment or capsicum tissue are of little value but a large kaolin poultice if well made does often give some relief and many patients derive comfort from them

Pain however severe can usually be controlled by sedatives and strapping but an artificial pneumothorax has been induced in cases where these resources failed and the pain has been especially excruciating Such occasions must be extremely rare and the operation under such conditions might produce empyema A linctus should be prescribed for the cough that often accompanies pleurisy and a sedative given at night

Convalescence is usually rapid, but the patient should not be allowed to resume work until fully restored to health and if a tuberculous origin is suspected prolonged treatment on sanatorium lines should be advised

Certain localisations of dry pleurisy require separate notice These are the diaphragmatic and interlobar forms

DIAPHRAGMATIC ACUTE DRY PLEURISY

Ætiology —This affection may occur under conditions similar to those causing dry pleurisy in other parts not infrequently it is secondary to pathological changes in the abdomen Thus hepatic cirrhosis perihepatitis perisplenitis hepatic abscess perinephric suppuration or peritonitis may lead to a spread of infection through the

diaphragm to the adjacent pleura It may also occur as a localised variety of secondary dry pleurisy, when the primary lesion is situated near the base of the lungs

Symptoms —Pain is usually very severe and may be referred to the shoulder or to the abdomen The former is caused by nociceptive impulses ascending the phrenic nerve to its origin in the third to the fifth cervical segments of the spinal cord leading to pain and hyperæsthesia referred to the cutaneous area of distribution of the fourth cervical root, at the summit of the shoulder The abdominal pain is in the epigastric and hypochondriac regions, and in addition there is a localised tender spot known as the " bouton diaphragmatique ' of Guéneau de Mussy This is situated in the subcostal plane, about 2 in from the mid line The diaphragm is nearly motionless on the affected side, and there is often some rigidity of the corresponding upper abdominal muscles Hiccough may be a noticeable and troublesome symptom The diaphragm, being nearly fixed in the inspiratory position may cause a slight downward displacement of the liver if the pleurisy is on the right side A pleural friction rub is rarely heard, the only abnormal signs commonly present being diminution of air entry and possibly slight dullness over the corresponding lower lobe of the lung

Diagnosis —This is often difficult, owing to the fact that the severity of the symptoms and their localisation frequently suggest the occurrence of some acute abdominal catastrophe such as perforation of a hollow viscus The abdomen should be most carefully examined in every case The history, the collapsed state of the patient and the evidence of free gas in the peritoneal cavity in perforation may assist in distinguishing between these conditions The symptoms however are not by any means always as severe as is suggested by the foregoing

Often this form of pleurisy can only be differentiated from ordinary pleurisy by the fact that the pain is made especially severe by any involuntary movement affecting the diaphragm such as laughing yawning, sneezing or coughing when the pain is like a knife thrust in the upper abdomen

Treatment —This is similar to that of simple dry pleurisy elsewhere save that morphine should be withheld until the diagnosis is conclusively established

INTERLOBAR DRY PLEURISY

Just as inflammation may be limited to the diaphragmatic portion of the pleura, so the membrane in the cleft between two lobes of the lung may be alone affected This does not give rise to definite symptoms and signs by which it can be diagnosed during life though its effects are not infrequently seen in radiograph films It is frequently discovered on necropsy, but is generally secondary to pulmonary tuberculosis or pneumonia and there is usually evidence of pleurisy elsewhere It only assumes clinical importance when followed by effusion and this condition is considered later

B CHRONIC DRY PLEURISY

Under this heading a variety of conditions are included Strictly, it should be restricted to those rare cases probably usually tuberculous in origin, in which the signs of dry pleurisy persist for long periods or recur at frequent intervals In such cases coarse dry friction may be heard over large areas of one lung often with little or no accompanying pain

Pleural adhesion and thickening are usually included in the group of chronic dry pleurisies There may be no symptoms or, at most slight dyspnœa on exertion with aching or pain on straining or on lifting weights Signs suggesting adhesion are local flattening and limitation of movement of the chest wall Litten s sign is also absent or diminished when the adhesion is basic, that is the shadow cast by the movement of the diaphragm best seen in the region of the seventh and eighth ribs in the anterior and mid axillary lines is not present or is much restricted The vocal

fremitus may be diminished and the percussion note impaired The breath sounds are often slightly weaker and the voice sounds may be diminished over the area where the thickening or adhesion exists

Chronic diaphragmatic pleurisy or adhesion may give rise to a group of symptoms simulating chronic gastric ulcer There is pain in the hypochondrium extending through to the back and aggravated by food Radiographic examination may be of value in demonstrating limitation of movement of one cupola of the diaphragm together with an angularity due to alteration of its normal contour Investigation of the gastric functions may also prove of value in diagnosis

The treatment of chronic dry pleurisy is mainly symptomatic.

C PLEURISY WITH EFFUSION

Many cases of pleurisy, possibly the majority, proceed to effusion The effusion is usually serous in character, but may be hæmorrhagic Inflammatory effusions must be distinguished from passive transudates which will be considered separately under the heading of hydrothorax

SERO FIBRINOUS PLEURISY

Ætiology —This is in the main identical with that of dry pleurisy of which it is, in effect a later stage It has now been established that the majority of cases of sero fibrinous pleurisy are due to the tubercle bacillus The evidence on which this conclusion has been arrived at is—(1) the subsequent history of the cases shows that a considerable proportion develop active lung signs within 5 years (2) the cytological and bacteriological examination of the exudate (3) post mortem examination of fatal cases (4) the results of tuberculin reactions

Other conditions which may give rise to serous effusions are lobar and lobular pneumonia pulmonary infarcts and new growth It may also occur in the course of generalised infections such as the enteric group acute rheumatism and septicæmia due to streptococci or staphylococci In most of these conditions the exudate often becomes purulent Inflammatory serous effusion may also occur as a complication of severe anæmias leukæmia chronic nephritis injury to the chest wall and inflammatory conditions below the diaphragm or in the pericardium It is also a common feature of polyorrhomeningitis

Pathology.—The affection commences with dry pleurisy spreading over the visceral and parietal pleura the fibrinous exudate soon forming a thick rough layer on the surface Further exudation of fluid occurs and accumulates in the pleural cavity the lung collapsing *pari passu* to accommodate it Owing to the hilar attachment of the lung it retracts upwards and inwards allowing the fluid to accumulate at the bases and in the axillary region where it reaches its highest level unless previously existing adhesions prevent it The lung retracts in this way owing to its elasticity until the pleural negative pressure is completely abolished In like manner the mediastinal contents including the heart, are displaced away from the affected side If fluid continues to be effused after the lung has retracted to the full extent and after the negative pressure has become abolished, a positive pressure is produced The lung is now compressed and the diaphragm with the liver and spleen are pushed down while the mediastinal structures are now displaced further towards the sound side In long standing cases the lung may undergo the change known as carnification as the result of the compression apneumatosis The lung appears dark red or slaty grey in colour, is firm airless and heavier than water If old adhesions are present, the effused fluid may be loculated and the collapse of the lung may be only partial

If there is much positive pressure collateral hyperæmia of the sound lung may result and progress to œdema The fluid in the pleural cavity is pale and clear it

often coagulates after withdrawal Its characters are further described on p 1070 The quantity may amount to as much as 5 or 6 pints

Symptoms —The onset is usually similar to that of dry pleurisy, but the constitutional symptoms are often more marked There may be an initial rigor but as a rule pain and dry cough are the earliest symptoms The fever is of moderate degree, although it may reach 103° F or more When effusion develops the pain is often relieved owing to the separation of the inflamed pleural surfaces If a large quantity of fluid is poured out rapidly, distress of another kind becomes apparent namely dyspnœa caused by the mechanical effects of the fluid, collapsing the lung and displacing the mediastinum In more slowly developing effusions there may be little or no dyspnœa, except on exertion Expectoration is not common unless there is coexisting pulmonary disease, or unless œdema of the sound lung develops

The patient often lies on the affected side or may be propped up in bed Cyanosis is not a marked feature even in large effusions, unless there is collateral hyperæmia of the sound side There is generally some prominence on the side of the effusion but the intercostal spaces are rarely bulged Movement is restricted or absent in the lower part of the chest on the affected side although with a moderate effusion the apical region may still expand The cardiac pulsations may be seen in an abnormal position, the impulse being displaced away from the side of the fluid In left sided effusions the pulsation may be most marked in the fourth space on the right side as far out as the nipple line On palpation the position of the impulse should be verified, and then the amount of chest movement and the character of the vocal fremitus determined The latter is diminished or completely absent over an effusion of moderate or large size, although it may be obtained over the area where the collapsed or relaxed lung is in contact with the chest wall The percussion note over the fluid is one of stony dullness and the sense of resistance is greatly increased The exact limits of this area of dullness should be determined with the patient sitting up and recumbent With moderate effusions the upper border of the dull area follows a curved line with the convexity uppermost known as the S shaped curve of Ellis or Damoiseau's line This is lowest at the back near the spine and reaches its summit in the mid axilla it then slopes downwards as it passes anteriorly towards the sternum In large effusions the dullness may extend up to the level of the clavicle and reach across the mid line of the sternum, moreover in left sided effusions it blends with the cardiac dullness, and the area of gastric resonance known as Traube s space may be encroached on or obliterated The relaxed lung above the effusion in front often yields a skodiac note which becomes dull if the quantity of fluid increases At the back there is a triangular area of impaired resonance or relative dullness above the stony dull area of fluid This is known as Garland s triangle It also corresponds with the relaxed or collapsed lung If the patient is examined while sitting upright there is often found at the base on the sound side opposite the effusion, a small area of dullness known as Grocco s triangle The base of this triangle extends outwards from the vertebral column along the lower margin of the lung for one to three inches the vertical side extends upwards at a right angle to the base, alongside the spinal column to about the highest level of the effusion, the hypotenuse joins these two lines This paravertebral dull area is caused by the bulge of the fluid forming the effusion Elsewhere over the sound lung the note may be slightly hyper resonant The area of deep cardiac dullness should be carefully marked out In left sided effusions it is displaced to the right and extends beyond the sternum in the third and fourth spaces even to the nipple or beyond it In right sided effusions, the displacement may be very obvious the left margin of the dullness extending as far out as the left mid axillary line The auscultatory signs are very variable, and much less characteristic than those obtained by palpation and percussion In some cases the breath-sounds over the dull area are distant and weak or even absent in others they are loud and bronchial or tubular This inconstancy probably depends upon

the extent of pulmonary collapse and the degree of patency of the bronchi With marked collapse and patent bronchi bronchial breathing is heard with partial collapse and obstructed bronchi the breath sounds are almost or quite abolished As a rule no adventitious sounds are heard but râles may be audible in the lung above the effusion Conduction of spoken voice is diminished or abolished but towards the upper part of the effusion and just above it the sound produced is heard distantly and with a peculiar nasal or bleating twang a condition known as ægophony The breath sounds heard under the clavicle over the relaxed lung above the effusion are frequently harsh or puerile In the contralateral lung the breath sounds may be vesicular or exaggerated and in cases of large effusions where there is marked circulatory obstruction there are frequently signs of congestion or œdema at the base Similarly pressure on the descending thoracic aorta may cause lowering of the blood pressure in the leg as compared with that in the arm (O K Williamson) There may be a systolic murmur over the cardiac region (displacement murmur) The abdomen should be examined to determine any downward displacement of the liver or spleen The blood count in sero fibrinous pleurisy rarely shows any leucocytosis apart from complications

Complications and Sequelæ—Acute œdema with albuminous expectoration is rare but is a dangerous condition unless treatment is prompt Permanent collapse and carnification of the lung may remain after absorption in prolonged cases and may progress to diffuse interstitial fibrosis More commonly some degree of pleural thickening and adhesion persists and expansion of the lower lobe may never be completely restored Sero fibrinous effusion due to tuberculosis rarely becomes purulent but this sequence is common in other forms Tracking of the fluid externally through the chest wall and rupture through the lung occur but rarely An infrequent complication is hemiplegia probably due to an embolus derived from a thrombus originating in a pulmonary vein Miliary tuberculosis occasionally follows rapidly on an effusion more commonly active tuberculosis of the lungs occurs after a lapse of some years

Diagnosis—The recognition of the presence of fluid in the pleural cavity is generally easy but with small or localised effusions it may be difficult The most valuable signs are the displacement of the heart the absence of vocal fremitus and the stony resistant dullness The auscultatory signs are of less value and may even be misleading The chief conditions which may simulate effusion are fibroid lung *with thickened pleura and bronchiectasis pneumonia particularly the massive form* malignant disease of the lung pleura or mediastinum massive collapse a large pericardial effusion and an aneurysm pressing on one or other main bronchus Subphrenic abscess may also give rise to difficulty (see Empyema) Fibroid disease can usually be recognised since there is generally flattening and sinking in of the affected side instead of bulging The heart if displaced is drawn towards instead of away from the affected side vocal fremitus is present although possibly diminished and the dullness is rarely of the stony character obtained over fluid The breath sounds *may be weak or bronchial and if bronchiectasis is also present the characteristically* variable signs of that condition should be helpful in diagnosis In massive pneumonia the differentiation may be difficult since breath sounds and voice sounds are sometimes completely absent if the bronchi are also occluded but the position of the cardiac impulse is generally of decisive importance In malignant disease and aneurysm careful observation should afford diagnostic indications such as glandular enlargement or abnormal pulsation and in both instances the radiograph may establish the diagnosis Malignant disease of the pleura may first show itself as a pleural effusion the tendency to recur after tapping the presence of blood in the effusion and the onset of emaciation may help to suggest the cause In massive collapse there is as a rule but little difficulty owing to the displacement of the cardiac impulse to the affected side In pericardial effusion the shape of *the cardiac dullness* may be sugges

tive, and the dislocation of the impulse may indicate the real condition, moreover the dullness over the lung behind is rarely of extreme degree unless pleural effusion coexists Radiographic examination is always desirable The shadow of fluid is generally dense, but does not obscure the rib shadows completely The upper level tends to be curved and shifts to some extent with the patient It merges into the shadow of the collapsed lung above The diaphragm is immobile on the affected side A further aid to diagnosis consists in exploratory puncture which has the advantage of establishing the nature of the fluid as well as its presence The technique of puncture is similar to that of paracentesis described below save that a hypodermic syringe with a Record 1 or 2 needle is often quite sufficient for diagnostic purposes Preliminary local anæsthesia by procaine (Novocain) or some similar preparation, should be employed in every case The same syringe and needle used for anæsthesia may also be used for the diagnostic puncture Serous pleural fluid of inflammatory origin varies in colour from pale greenish-yellow to brown The specific gravity is usually 1 018 or over Protein is present as serum albumin serum globulin and fibrinogen, the total quantity being as a rule over 4 per cent The fluid generally clots spontaneously after withdrawal The cytology of the fluid is varied showing lymphocytes, polymorphonuclear cells, erythrocytes and altered endothelial cells in varying proportions A marked preponderance of lymphocytes is very suggestive of a tuberculous origin while the presence of large numbers of polymorphonuclear cells is usually an indication of some other infection, generally by a pyogenic organism In rare cases large numbers of eosinophils have been found The origin of these cases of so called eosinophil pleurisy is at present doubtful Cultural examination of tuberculous fluid usually proves sterile unless Loewenstein s or Dubos medium is used, but in fluid from other causes the infecting organism can often be grown To establish the tuberculous nature of a pleural fluid, inoculation of 15 ml of the fluid into a guinea pig may be tried The methods of differentiation of an inflammatory exudate from a passive transudate are given on p 1076

Course—In effusions of moderate size the temperature usually subsides in from 7 to 10 days, and spontaneous absorption is complete in 2 3 or 4 weeks In large effusions reaching up to the second rib or higher, the course may be less favourable The fever may persist even for weeks and absorption of the fluid may be slow or wanting entirely Aspiration may accelerate the resolution, and usually only one tapping is necessary, the fluid left behind being absorbed rapidly In rare cases fluid reaccumulates quickly after repeated tappings and a so called inexhaustible effusion occurs In some such patients fluid may remain in the pleura for the rest of life

Prognosis—The immediate prognosis is good, although with large effusions of 4 pints or more, sudden death sometimes occurs from acute œdema of the lungs cardiac failure or embolism The ultimate result depends on the cause In non tuberculous effusions recovery may be complete, save for pleural adhesion or they may progress to empyema In tuberculous effusions arrest may remain complete but, as already stated a considerable proportion of the cases develop pulmonary disease after years

Treatment—Paracentesis can be carried out in various ways The simplest method is that of siphonage a long rubber tube filled with sterile saline solution is attached to a trocar and cannula which are passed into the pleural cavity and the fluid is siphoned into a receptacle at a lower level This method has the great advantage that the degree of suction employed is under control and the lungs expand gradually as the fluid is withdrawn When this method works it is very effective but it sometimes fails for various reasons A double acting syringe or a syringe with a two way tap is more often used and some still use Potain s apparatus which is effective if the corks and connections are in good condition

In performing aspiration the patient should sit up in bed or lie slightly turned

on to the unaffected side The skin should then be prepared as for an operation and the whole procedure should be carried out as a sterile operation The skin and muscles should be well infiltrated down to the pleura with procaine 2 per cent and the needle used for the anæsthetic should be pushed into the pleural space to make certain that anæsthesia is complete and to confirm the position of the fluid A sharp needle or a small trocar and cannula should be pushed into the pleural space just above a rib *in order to avoid the intercostal artery on the under surface of the rib* above The site chosen depends on the position of the fluid but the most convenient ones are the sixth space in the mid axilla the seventh space in the posterior axillary line or the eighth space just below the angle of the scapula Aspiration should be stopped if cough occurs or the patient complains of any general malaise or discomfort Aspiration is exhausting to the patient so should not be too prolonged Removal of 1 to 2 pints is all that it is safe to remove at one aspiration and removal of more and too rapid removal of as much may produce œdema of the lung and albuminous expectoration by affecting the pulmonary circulation Removal of only part of an effusion sometimes seems to accelerate the absorption of the whole probably by the chain effect of increasing mobility One of the risks of paracentesis is said to be sudden death from pleural shock Sudden death does very occasionally occur but is probably due to air embolism a risk inseparable from the use of a hollow needle Other risks are also due to faulty technique and comprise entrance of air into the pleural cavity from ill fitting needles or wrong connections or from puncture of the lung

The operator must always keep in mind the danger of infecting the pleural cavity through a failure in sterility

Exploratory puncture is advisable to permit the examination of the fluid Opinions differ somewhat as to the indications for paracentesis which however is nowadays performed earlier and more frequently than was formerly the case It is unnecessary in cases in which absorption of the fluid is apparent within 10 days The following conditions may be considered to suggest its employment (1) if the effusion is large and causing positive pressure as shown by dullness up to the clavicle marked dyspnœa downward *displacement of the liver or spleen and collateral hyperæmia of the sound* lung (2) if absorption is slow the fluid remaining at the same level for a fortnight or more (3) if acute œdema with albuminous expectoration occurs (4) in cases of bilateral effusion with increasing dyspnœa the side with the larger effusion may be aspirated (5) if the effusion is accompanied by persisting high temperature and constitutional symptoms

The old cliche that the pleural effusion is Nature s splint and other old saws have been responsible for a great deal of unnecessary permanent disability as a result of not aspirating large effusions Generally speaking large effusions should be aspirated early and the aspiration repeated if necessary Often however the aspiration of a moderate amount of fluid facilitates the reabsorption of the rest through increasing the momentum of the pulmonary movements There are, however still many different opinions on the subject of whether or not to aspirate a tuberculous effusion It has long been a common custom to leave the effusion unaspirated on the ground that it acts as a form of collapse therapy There is no evidence that this is true and it is certain that this belief leads to unnecessary discomfort and avoidable disability If collapse therapy is necessary in these cases air replacement would be a more logical and effective remedy

General Management —Patients with large effusions should be nursed propped up on pillows they should be discouraged from sudden lateral alteration in position as the sudden displacement of the mediastinum may cause distress and cardiac embarrassment The patient should be told that he will be away from work for not less than 6 months For about the first 3 months he should be kept in bed although if the fluid has reabsorbed and the temperature and the sedimentation rate have been normal for 3 weeks he may get up by degrees towards the end of the period He

should spend the next 3 months in the most healthy circumstances possible observing daily rest and early hours During all this time he must be under strict radiological control which will be necessary for at least 5 years The radiographs should be monthly at first then 3 monthly and eventually at 6 months intervals The convalescence of some patients will be delayed by persistence of temperature or fluid or both

Since statistics show that between 20 to 30 per cent of pleural effusions are followed by pulmonary tuberculosis inside 5 years and since streptomycin has been found to be most effective in recent presumably vascular lesions it appears logical to treat these patients with it during their period of rest Streptomycin in daily doses of 1 g should be given in two courses of 21 doses, separated by 14 days interval To diminish the likelihood of producing streptomycin resistance isoniazid in 100 mg doses twice daily should be given at the same time as the streptomycin

ANOMALOUS PLEURAL EFFUSIONS

Two unusual forms of pleural effusion require brief mention—they are encysted interlobar and encysted diaphragmatic sero fibrinous pleurisy The former can only be recognised by radiographic examination followed by exploratory puncture Encysted diaphragmatic sero fibrinous pleurisy is rare, but a case has been erroneously recorded as acute serous mediastinitis This condition is simply one of pleural effusion localised to the space between the mediastinal pleura, the diaphragm and the lung Both of these conditions if diagnosed, should be treated on general principles The effusion may absorb spontaneously but if not, aspiration may be necessary

PURULENT PLEURISY (EMPYEMA)

In this condition the pleural exudate becomes purulent The fluid may be turbid and the presence of pus be apparent only on microscopical examination, or it may consist of typical pus

Ætiology —Predisposing Causes —Empyema is common in children under 10 years of age, and the younger the child the greater the probability that any effusion will be purulent In adults it is commonest between the ages of 20 and 40 years, probably owing to the heavy incidence of pneumonia in this age period Purulent pleurisy is but rarely primary except in the form due to the pneumococcus It is most commonly due to extension from the lungs especially from lobar pneumonia and from broncho pneumonia Other pulmonary causes are tuberculosis, bronchiectasis, abscess gangrene new growth or septic infarcts in infective endocarditis It may develop in association with mediastinal lesions, such as suppurating glands ulcerating carcinoma of the œsophagus or from suppuration in the neck tracking downwards Infection of the pleura may occur through the chest wall as a result of gunshot wounds stabs, fractured ribs and faulty technique in aspiration of a serous effusion The primary source of pleural infection may be in the abdomen, the organisms passing through the diaphragm from a perinephric subphrenic or hepatic abscess, or from localised or generalised peritonitis consequent on rupture of a gastric or duodenal ulcer The involvement of the pleura may take place through the blood in septicæmia suppurating gunshot wounds compound fracture of the femur and in otitis media with lateral sinus thrombosis

Empyema may develop during the course of many of the acute specific fevers such as scarlet fever variola measles and the enteric group, but since in these conditions it is usually secondary to broncho pneumonia it belongs strictly to the pulmonary group

EXCITING CAUSES —The organisms most frequently found in purulent effusions are the pneumococcus and the streptococcus the former accounting for more than

half of the cases Occasionally the pus proves to be sterile on culture such cases are generally the result of the tubercle bacillus or of a pneumococcus which has died out Other organisms less commonly found are staphylococci *H influenzæ Salm typhi Bact coli* and Friedlander s bacillus Streptothrix organisms are occasionally found (see Actinomycosis) also various saprophytes and anaerobic organisms especially in fetid empyema

Pathology—The initial stages are similar to those of dry and sero fibrinous pleurisy but when the effusion occurs it proves to be rich in leucocytes undergoing disintegration and to contain the infecting organism It varies from a slightly turbid semi translucent fluid to typical thick opaque creamy pus Its colour ranges from pale amber to green or greenish grey It may be odourless or extremely offensive In cases secondary to gangrene it may be thin and horribly fetid while in pneumococcal cases it may be curdy and of slightly sweetish odour The pleura is covered with a more or less thick layer of sodden fibrinous exudate In cases due to the pneumococcus this false membrane may be very thick Adhesions form quickly leading to encystment or loculation of the pus Such adhesions also prevent the lung from expanding after evacuation of the pus with the result that the lung becomes carnified and interstitial fibrosis results There is usually some enlargement of the bronchial glands In long standing cases there may be lardaceous disease of the liver, spleen kidneys and intestines

Symptoms—Since empyema usually develops in the course of or as a sequel of some other disease its symptoms are often masked by those of the primary disease and may easily be overlooked In primary cases due to the pneumococcus the onset may be like that of pneumonia in the more common secondary cases a rise of temperature and increase of signs develop after the crisis In general it may be stated that the symptoms are similar to those of sero fibrinous pleurisy but more severe There is more malaise and the patient may appear profoundly ill with rigors sweats and dyspnœa The temperature ranges higher up to 103 F or more and may be of septic type with marked daily remissions but some cases are almost if not completely apyrexial The signs are usually exactly similar to those of sero fibrinous effusion but in some instances special features may be noticed In neglected or prolonged cases wasting pallor and cachexia become marked The intercostal spaces may be found to bulge and œdema of the chest wall is sometimes apparent The pus may track through an intercostal space generally the fifth near the nipple producing a fluctuating swelling known as a pointing empyema or *empyema necessitatis* This may infiltrate the skin and simulate a superficial abscess The swelling so induced may pulsate especially if it be on the left side—a condition known as pulsating empyema Pulsation communicated to the chest wall may also be observed in some large left sided purulent effusions without local swelling The displacement of the liver or spleen may be greater than with serous effusions probably owing to the higher specific gravity of the pus which is usually 1 030 or more and to the associated inflammation of the diaphragm In fetid empyema the breath and sputum may be offensive even before rupture into a bronchus occurs Clubbing of the fingers and toes occurs in empyema of long standing but may develop in a few weeks Blood examination reveals a moderate leucocytosis in the majority of cases Counts of 15 000 leucocytes per cubic millimetre are usual and in some instances figures up to 100 000 per cubic millimetre are obtained

Complications and Sequelæ—In neglected or untreated empyema the pus may track and become discharged in various directions The commonest is rupture through the visceral pleura into the lung and discharge through a bronchus This may lead to sudden death from suffocation on the other hand in small empyemata spontaneous cure may follow this evacuation of the pus In other instances pyo pneumothorax results and occasionally gangrene of the lung A second method of discharge is through the chest wall as an *empyema necessitatis* Perforation may

occur into the pericardium, or into the œsophagus with the formation of a pleuro œsophageal fistula The diaphragm may be perforated with the production of a sub phrenic, lumbar or psoas abscess, while in other cases general peritonitis may ensue

The pericardium or the mediastinum may become infected without perforation similarly costal periostitis may be induced After spontaneous or operative evacuation the cavity may fail to close and a chronic empyema or sinus result This is generally due to the lung being permanently collapsed and adherent and therefore failing to expand It subsequently undergoes fibrosis with development of bronchiectasis Sometimes the failure to close may be due to the nature of the infection particularly when it is due to tuberculosis or actinomycosis In other cases it may be due to a bronchial fistula or to a foreign body in the pleura Generalised infection is rare but cerebral abscess, probably of embolic origin, is not very uncommon especially in cases due to streptococci Chronic pulmonary osteoarthropathy is an occasional complication, and lardaceous disease sometimes occurs in cases of long duration Diphtheritic infection of the wound, with subsequent paralysis has been recorded after operation, more especially in cases secondary to influenzal broncho pneumonia

The sequelæ in untreated cases may be fistulæ such as pleuro bronchial pleuro œsophageal or external, and various deformities The sequelæ after operation may be a small amount of pleural thickening or if operation were delayed and re-expansion incomplete there is falling in of the chest, with flattening dropping of the shoulder and secondary scoliosis In other cases, as mentioned above, a chronic sinus may result.

Diagnosis —The diagnosis of empyema involves two distinct problems—one the recognition of the presence of fluid in the pleura which is considered under sero fibrinous pleurisy the other the demonstration of its purulent character In spite of the more severe symptoms, empyema is frequently overlooked even by physicians of experience This is partly due to the fact that its development may be insidious with signs increasing but little from day to day, and partly to its secondary character, its onset being obscured by the clinical features of the primary condition It is wise therefore to suspect its existence in any case of obscure lung signs especially those with dullness, cardiac displacement and fever, consequent on pneumonia of any variety

There are a few special difficulties as compared with sero fibrinous effusion which merit separate mention The first of these is subphrenic abscess This may lead to immobilisation of the diaphragm on one side more commonly the right, and cause collapse of the lung and even pleural effusion The difficulty is greater when the subphrenic abscess contains gas as well as pus The history the absence of displacement of the heart s impulse and radiography may all assist but the differentiation is often extremely difficult

Empyema necessitatis may simulate a tuberculous or other abscess about a rib and empyema should always be suspected in any case of local fluctuant swelling about the chest wall Pulsating empyema requires to be distinguished from aortic aneurysm the pulsation is less forcible and little if at all expansile in the former The cardiac displacement the radiograph and cautious exploratory puncture enable the nature of the condition to be recognised

In any case in which empyema is suspected three examinations may be under taken—a blood count radiographic investigation and exploratory puncture A poly morphonuclear leucocytosis of 15 000 per cubic millimetre and over a dense shadow in the radiograph obscuring the ribs together with cardiac displacement may be very suggestive while puncture may prove the presence of pus Sometimes however puncture may fail although pus is present This may be due to the pus being too thick to pass through the needle to loculation of the pus or to wrong choice of the site for puncture The latter explanation is usually the real one since quite thick pus will often pass through quite a thin needle In this case if

the other signs indicate pus repeated punctures with a larger needle under anæsthesia are called for but it is well to be prepared to proceed to operation if pus is found

Course —Apart from spontaneous cure of small empyemata by inspissation of the pus or discharge through a bronchus or through the chest wall death generally occurs in untreated cases within a month or two As in sero fibrinous pleurisy sudden death may occur Death may occur after operation from exhaustion or from cerebral abscess

Prognosis —This depends upon the primary cause the method of treatment adopted and the duration of the effusion before the operation The most favourable forms are those due to the pneumococcus which are recognised and treated at an early stage In neglected cases with profound toxæmia, with gangrene of the lung or lardaceous disease the outlook is extremely grave Empyemata due to streptococcal infection are serious unless recognised early similarly with cases of fetid empyema due to anaerobic infections Infected hæmothorax consequent on gunshot wounds of the chest is of grave prognosis The outlook is serious in cases of bilateral empyema but recovery may follow evacuation of the pus on the two sides

Treatment —The pus aspirated should be sent for cultivation and the organisms identified and examined for sensitivity to various antibiotics In the meantime as much of the pus as can be conveniently and comfortably removed should be aspirated and in the absence of more definite information as to the susceptibility of the organ isms up to 500 000 units of penicillin should be put into the pleural cavity at the end of aspiration Cultivation of the organisms may show that other antibiotics would be more appropriate if there are to be subsequent aspirations

Some cases of empyema may clear up with aspiration and antibiotics alone but it is wise to assume that operation will probably be necessary when the empyema has become localised in the chest Indications that suggest that operation might not be necessary would be that the fluid showed signs of disappearance, that the fluid had become sterile and from being purulent and thick was becoming serous and thin while the leucocytosis and temperature had subsided Neglected or missed empye- mata are rarely seen in Great Britain nowadays but the desperately ill case with a large empyema is often best treated at first by the use of a trocar and cannula and the insertion of an intercostal catheter which is led off into a drainage bottle with a water seal Controlled drainage of this sort is less exhausting to these patients than aspiration, and soon makes them fit for operation which would probably have been fatal beforehand

Before the use of antibiotics treatment consisted in the evacuation of the pus by operation as soon as the diagnosis was established in pneumococcal cases In those of streptococcal origin operation was not resorted to while the fluid was of thin sero purulent character but was postponed until it was definitely purulent Premature operation in streptococcal cases has been shown by the American Empyema Commission to be a very dangerous procedure since the fluid is not shut off by adhesions and operation may lead to open pneumothorax with flapping mediastinum At this stage the condition is described as pyothorax A preliminary aspiration is of advantage in large effusions and may be repeated in streptococcal effusions until they are ready for operation The operation consists in drainage by removal of a piece of rib subperiosteally and incision of the parietal pleura

In cases of chronic empyema or of sinus failing to close the question of some plastic operation must be considered Various forms of operation have been devised involving removal of portions of many ribs and the decortication operation of Fowler and Delorme The general condition of the patient must be carefully considered before these operations are advised

Special Varieties of Empyema —Certain special localisations of purulent pleurisy require separate consideration notably apical interlobar and diaphragmatic empyemata

Apical empyema —This condition is usually secondary to apical pneumonia less

commonly to pulmonary tuberculosis It is one variety of encysted empyema the pus being shut off from the rest of the pleural cavity by *adhesions* The symptoms and signs are not characteristic but may be suggestive There is very marked dullness below the clavicle, *not* transgressing the middle line with weak or absent breath sounds and possibly some indications of mediastinal displacement Diagnosis can as a rule be established only by the radiograph and exploratory puncture, the latter being carried out in the second space near the mid clavicular line The treatment consists in drainage by incision as near the lower limit of the effusion as possible

Interlobar empyema—Pus collecting between two of the lobes may be difficult to differentiate from pulmonary abscess, gangrene and bronchiectasis It is often not diagnosed until rupture into a bronchus draws attention to it The signs are generally most marked in the axilla or near the angle of the scapula They are often slight until rupture occurs, and even then there may be only a small area of dullness in the line of an interlobar fissure, with distant or weak bronchial breathing and a few rales The pus expectorated may be fetid, and the patient s breath may be offensive a few days before rupture occurs The condition simulates abscess of the lung and may be almost impossible to differentiate from that affection Radiographic examination gives the greatest help in the diagnosis Recent observations suggest that interlobar empyema is much less common than abscess The treatment is identical with that for pulmonary abscess

Diaphragmatic empyema—The pus is usually encysted and may be so deeply situated as to give but few signs The initial symptoms are generally severe, being those of diaphragmatic pleurisy but hiccough is often a troublesome feature When pus forms there may be marked constitutional symptoms, and obscure signs may develop, such as dullness at a point just above the base behind, with weak or distant bronchial breathing With such a history and obscure basic signs especially when they occur *after* an attack of pneumonia the use of the radiograph and of the exploring needle should not be neglected In cases not recognised and treated, rupture into a bronchus or through the diaphragm may occur The treatment is similar to that for ordinary empyema

HYDROTHORAX (DROPSY OR HYDROPS OF THE PLEURA)

Hydrothorax is the name applied to a collection of clear fluid in the pleural cavity the result of passive transudation from the capillaries

Ætiology—The commonest cause of hydrothorax is cardiac failure It occurs in acute and chronic renal disease, under conditions similar to those leading to dropsy in these affections It is sometimes found in severe *anæmias* *especially pernicious anæmia* Obstruction to the azygos veins may lead to transudation into one pleural cavity or into both This obstruction may be induced by *pressure from without* by a mediastinal or pulmonary new growth or by internal causes such as thrombosis An ovarian fibroma may be complicated by ascites and hydrothorax, a condition known as Meigs syndrome

Pathology—The pathology of hydrothorax is that of dropsy elsewhere It is produced by mechanical or chemical conditions affecting the blood flow through the capillaries, and it must be distinguished carefully from inflammatory effusion There is a difference in the composition as well as in the origin of the two kinds of pleural fluid The characters of inflammatory effusions have been described under pleurisy with effusion The fluid in hydrothorax is pale yellow in colour and the specific gravity is 1 015 to 1 010 or less It is clear and does not clot after removal There is little protein often not more than 1 per cent but transudates due to local obstruction may contain as much as 3 per cent The cellular elements are scanty although some endothelial cells may be present often united together in plaques The fluid may be definitely blood stained when it is described as hæmo hydrothorax

Hydrothorax is usually bilateral in cases due to cardiac or renal disease but in the former there is often more fluid on the right side or the fluid may be confined to that side The explanation of this is somewhat obscure It has been suggested that it is due to pre sure or traction on the vena azygos major by the enlarged right heart but according to Fetterolf and Landis a more likely explanation is pressure of the distended right auricle upon the pulmonary veins Fluid may also collect in greater quantity on the side upon which the patient lies most constantly In cases with unilateral pleural adhesion œdema of the lung may occur on that side while hydrothorax occurs upon the other

Symptoms—The symptoms of hydrothorax are generally overshadowed by those of the condition causing it but the occurrence of dyspnœa and cyanosis in any case of cardiac or renal disease should suggest careful examination of the bases of the lungs In the absence of inflammatory complications the condition is afebrile The signs are identical with those of sero fibrinous pleurisy save that no friction sounds are audible at any stage It is however more difficult to assess the signifi cance of displacement of the cardiac impulse owing to the increased size of the heart in the cases of cardiac origin

Diagnosis—This depends upon the presence of signs of fluid in the pleura in association with cardiac or renal disease with absence of fever and also upon the characters of the fluid withdrawn by puncture or aspiration Meigs syndrome is liable to be mistaken for a malignant ovarian tumour

Treatment.—Removal of the fluid may give great relief It may be necessary to repeat the operation since the fluid often reaccumulates The treatment of the primary condition should also be carried out. Mercurial diuretics are sometimes effective and may be given where there is no evidence of renal disease

HÆMORRHAGIC PLEURAL EFFUSIONS

All fluids poured out into the pleura contain a certain number of red blood corpuscles It is only when a number sufficient to give a definite red colour is present that the fluid is regarded as hæmorrhagic

For convenience of description three forms may be differentiated—(1) Hæmor rhagic pleurisy or hæmo serothorax (2) hæmo hydrothorax and (3) hæmothorax

1 Hæmorrhagic pleurisy

This is simply a pleurisy with effusion in which the exudate is blood stained

Ætiology—The usual causes are malignant disease of the lungs pleura or medi astinum and sometimes tuberculosis of the lung and pleura Hæmorrhagic pleurisy may occur in association with hepatic cirrhosis but in this case it is often the result of a terminal tuberculosis It occurs less frequently in association with blood diseases such as purpura and with the malignant or hæmorrhagic varieties of acute infectious fevers such as scarlet fever and small pox and occasionally with lobar pneumonia Sometimes in tapping a sero fibrinous effusion for the second time it is found that the fluid which was originally clear is now blood stained This is not necessarily an indication of increase in the severity of the process but may be due to injury of a blood vessel at the first operation

Symptoms—The symptoms and signs are identical with those of serous effusion and the hæmorrhagic character can only be recognised by withdrawal of the fluid An interesting point is the frequency of excess of eosinophils in these effusions Diag nosis and treatment are the same as for sero fibrinous pleurisy

2 Hæmo hydrothorax

This condition has been referred to under hydrothorax It consists simply in blood staining of a passive transudate into the pleura

3 HÆMOTHORAX

Hæmorrhage into the pleural cavity is the result of injury or disease of the vessels of the lung, mediastinum or chest wall

Ætiology—The chief causes are injury such as penetrating chest wounds or fracture of the ribs rupture of an aneurysm and erosion by new growth Experience of the traumatic group has been largely increased during the War of 1914–1918 and the War of 1939–1945 Hæmothorax was noted in about 70 per cent of chest wounds Occasionally it occurs after the spontaneous rupture of adhesions and it is a rare complication of artificial pneumothorax treatment and a less rare complication of adhesion section in pneumothorax treatment

Pathology—The effused blood generally comes from the lung vessels, less commonly from the intercostals It is 'whipped' by the movements of the heart and lungs with the result that fibrin is deposited in layers upon the diaphragmatic pleura and the parts of the visceral and parietal pleura in contact with the blood The fluid remaining in the pleura or withdrawn by aspiration is largely defibrinated and therefore does not clot unless a secondary pleurisy develops

The lower lobe of the lung on the affected side becomes collapsed and eventually carnified unless absorption occurs or unless the blood is aspirated The upper lobe may show some compensatory emphysema and adhesions may form in the pleura separating it from the hæmothorax below When secondary infections of the bronchi or lungs occur, such as bronchitis or broncho pneumonia the collapsed lower lobe is not affected

Symptoms—The symptoms of hæmorrhage into the pleura from medical causes, such as rupture of an aneurysm or erosion of a large vessel are collapse and rapid death When due to disease or injury of an intercostal vessel, they may be insidious and slowly ingravescent until dyspnœa restlessness and the other indications of internal hæmorrhage develop When due to injury similar symptoms occur but may be masked or overshadowed by the shock, hæmoptysis and cough induced by the wound of the lung or chest wall The signs are those of pleural effusion, but in traumatic cases certain special features may be mentioned There is a great tendency to retraction of the chest wall on the affected side and the cupola of the diaphragm on this side is displaced upwards Irritation of the diaphragmatic pleura by the presence of blood may cause rigidity of the upper abdomen which sometimes gives rise to an erroneous diagnosis of intestinal perforation Vocal fremitus is usually diminished or absent Breath sounds will usually be absent but bronchial breathing may be heard and in these cases the voice conduction is also increased

Complications and Sequelæ—The most serious complication is infection of the effusion This is generally due to organisms introduced at the time of the wound either by the missile or by portions of the clothing or skin carried in with it Aerobic organisms such as a streptococcus or anaerobic ones as the *Clostridium Welchii* or *Cl sporogenes* may be present A hæmo pneumothorax may develop the gas entering the pleural cavity from the wound in the lung or through the chest wall Gas may also be formed by gas producing infecting organisms in the effusion Massive collapse may occur in the contralateral lung or other complications may arise such as bronchitis broncho pneumonia lobar pneumonia or œdema of the lungs If the effusion is small and not infected there are usually no permanent after effects In severe cases sequelæ similar to those of sero fibrinous pleurisy and empyema may result

Diagnosis—Hæmothorax should be suspected when basic dullness develops shortly after a gunshot wound of the chest The mistake that is most likely to be made in such cases is to confuse hæmothorax with lobar pneumonia The cardiac displacement and the diminution of vocal fremitus over the dull area are the most valuable diagnostic signs An active lobar collapse is distinguished by the fact that

the heart is displaced towards the affected side Radiography affords valuable confirmatory evidence in most cases When air and blood are present the upper border of the dark area in the radiograph has a sharply defined edge while the pleural cavity above is very translucent The use of the exploring syringe generally settles the diagnosis except in certain cases in which although a considerable quantity of blood may be present none is removed by aspiration owing to the needle entering the clot

Course—This depends upon the cause and size of the hæmothorax, and upon the mode of treatment adopted It is profoundly and gravely influenced by infection of the effused blood A small sterile hæmothorax is generally absorbed spontaneously Medium sized and large effusions may not disappear unless aspirated An infected hæmothorax will inevitably prove fatal if untreated

Prognosis—In a sterile hæmothorax due to a chest wound the prognosis is good If infection occurs the prognosis depends upon the promptitude with which this condition is recognised and radically treated

Treatment—The blood in the pleural cavity and the fluid exuded from the pleura in response to the irritation of the blood form an ideal culture medium for infecting organisms All hæmothoraces should therefore be aspirated at short intervals until the pleura remains dry It is probable that the blood in the pleural space clots in most cases quite quickly that it is then defibrinated by the whipping effect of the movement of the heart and lungs then the fibrin sinks to the bottom of the pleural space on the diaphragm or is deposited on the pleura and pericardium The defibrinated fluid can be aspirated and its presence causes dilution with serous fluid until eventually the fluid becomes clear and yellow as the percentage of blood falls Incidentally the serous effusion contains fibrinogen so that the whole contents may clot again unless they are aspirated Such a clot becomes organised and forms a thick fibrous lining on the visceral and parietal pleura which impedes re expansion In such cases thoracotomy to evacuate the clot and decorticate the pleura is necessary

In view of the danger of infection it is wise to give penicillin or the sulphonamides from the start If infection takes place, treatment is the same as that for empyema (*q v*)

Hæmothorax due to rupture of adhesions or to trauma may on occasion cause severe blood loss and thoracotomy accompanied by transfusion may be necessary in order to find the bleeding point and save life Patients should be given adequate doses of iron but it is often wise to start convalescence with a transfusion of blood

CHYLOUS AND OTHER MILKY EFFUSIONS

A milky fluid is occasionally obtained on exploratory puncture or aspiration of a pleural effusion It is usual to classify such fluids into three groups—(1) Chylothorax (2) chyliform fluid (3) pseudo chylous fluid

1 CHYLOTHORAX

There is an effusion of pure chyle or of serous fluid mixed with chyle

Ætiology—Chylothorax is usually the result of injury to or disease of the thoracic duct The traumatic form is as a rule, secondary to crushing of the chest wall with fracture of the ribs In disease, the thoracic duct may be pressed on by a malignant growth or enlarged mediastinal glands or the flow may be obstructed by thrombosis of the left subclavian vein Invasion of the thoracic duct by *Filaria bancrofti* may also be a cause

Pathology—The fluid in true chylothorax is a milky emulsion which remains so on standing although a cream like layer may form at the top With the microscope fat globules can be seen, which stain with the usual fat stains and can be dissolved by ether

2 CHYLIFORM EFFUSION

In this condition fat is present but it is not derived from the thoracic duct.

Ætiology —Chyliform effusions occur in association with tuberculosis and carcinoma of the pleura or lung

Pathology —The fluid is milky and contains fat in emulsion although in smaller quantities than in true chylothorax On microscopical examination large fat droplets are seen and numbers of cells, chiefly leucocytes undergoing fatty degeneration It is no doubt, from this process that the fat is derived

3 PSEUDO CHYLOUS EFFUSION

In this condition the milky appearance is not due to fat but to other particles causing opalescence

Ætiology —Pseudo chylous fluid has beeen observed in chronic effusions due to heart disease nephritis tuberculosis and malignant disease

Pathology —The milky appearance is due in some cases to a lecithin globulin complex (Wallis and Scholberg) Other rare causes of milky opalescent or turbid effusions are the presence of particles of calcium phosphate cholesterin or filarial embryos These fluids are distinguished from the above by showing a deposit on standing

Diagnosis —This can only be established by microscopical and chemical investigation of the fluid withdrawn

Prognosis —The prognosis in most cases of milky effusions is serious owing to the gravity of the primary condition Some traumatic cases of true chylothorax recover

Treatment —The treatment is for the most part symptomatic and dependent upon the primary condition In true chylothorax removal of the fluid is inadvisable, unless it is causing dyspnœa or other symptoms of pressure The drain of fat caused by it is a serious loss especially if the tapping has to be repeated frequently In chyliform effusions there is a marked tendency to recur after removal of the fluid

PNEUMOTHORAX

In pneumothorax, gas, usually air collects between the layers of the pleura, which now becomes a real instead of a potential space When serous fluid is present as well as the gas it is called a hydro pneumothorax when pus forms the condition is described as pyo pneumothorax and when blood and gas collect the term hæmo-pneumothorax is applied

Ætiology —Pneumothorax is more common in men and the maximum incidence is between the ages of 20 and 40 years but it may occur at any age The air may gain access to the pleural cavity in the following ways (1) Through the visceral pleura from the air in the lungs and bronchi This accounts for 95 per cent or more of the cases The commonest cause is probably the rupture of a subpleural emphysematous vesicle Pulmonary tuberculosis is a much less common cause, although the ruptured vesicle may be in the scar of a healed lesion Since emphysema is an almost invariable concomitant of asthma and the severe pneumoconioses spontaneous pneumothorax is a not uncommon complication in these conditions although the diagnosis is more often made by radiological examination than by any other way Other pulmonary causes are rupture of an empyema into the lung gangrene of the lung or pulmonary abscess rupturing into the pleural space Accidental puncture of the lung during paracentesis is an extremely common event A broken rib perforating the lung can also induce it It may also occur as a complication of artificial

pneumothorax treatment especially when this is bilateral (2) Through the chest-wall as a result of penetrating wounds although pneumothorax is not a common result. An abscess in the chest wall opening externally and through the pleura or a discharging *empyema necessitatis* may be a cause (3) Through the mediastinum by ulceration of an œsophageal growth or of a diseased bronchial gland into the pleura or from accidental perforation of the œsophagus during the passage of an œsophageal bougie or œsophagoscope (4) Through the diaphragm from some hollow abdominal viscus *e g* an ulcer of the stomach or duodenum may perforate leading to the formation of a subphrenic abscess which in turn may break through the diaphragm into the pleura or through therapeutic pneumoperitoneum where there is a congenital pleuro peritoneal sinus (5) Gas may accumulate in the pleura owing to infection of a pleural effusion by gas producing organisms This is generally the result of wounds

Sudden spontaneous pneumothorax in apparently healthy persons is not very unusual and is occasionally found in the course of routine radiography It is usually known as simple benign pneumothorax The causation is not certain but it used to be regarded as tuberculous with the same significance as a pleural effusion this belief has now been discarded Brock performed thoracoscopy in some of these cases and in a proportion of them he was able to see ruptured vesicles in either generalised or localised emphysematous areas In some he found ruptured bullæ in apical scars presumably tuberculous in some a cystic appearance of the lung and in others a peculiar cuckoo spit appearance which leaked air The probability is that in the majority of cases benign spontaneous pneumothorax is due to the rupture of an emphysematous bulla however caused In most cases the lung rapidly re expands although there is a tendency to recurrence usually on the same side but occasionally on the opposite side Complete recovery is the general rule although in rare cases re expansion takes a long time and may not occur Very occasionally spontaneous hæmopneumothorax occurs The symptoms are usually more severe and a fatal result is not uncommon

The exciting cause of pneumothorax may be physical strain or violent cough but many cases occur while the patient is at rest or even during sleep

Pathology—The entrance of air between the layers of the pleura disturbs the pressure relations in the thorax in a similar way to the effusion of fluid but whereas with the latter the process is gradual in pneumothorax it is rapid and the pressure within the pleura changes from the normal negative figure to that of the atmosphere often in a few minutes or less Mediastinal and cardiac displacements like those in pleural effusion and due to the unopposed traction of the sound side are also rapidly produced The subsequent pressure relations depend upon the source of the air If the opening is in the chest wall the intrapleural pressure will remain equal to the atmospheric until the opening becomes closed If the opening is in the lung three varieties occur (1) the opening may remain patent when the pressure keeps at atmospheric level (2) the opening may be valvular permitting the entry of air into the pleura during inspiration but preventing its escape during expiration In this case the pressure in the pleura rises above that of the atmosphere and the air within it is at a positive pressure causing further cardiac and mediastinal dislocation with downward displacement of the diaphragm (3) the opening becomes sealed and there is a condition of closed pneumothorax in which the pressure may be equal to greater or less than that of the atmosphere

To demonstrate pneumothorax post mortem the necropsy may be performed under water or by a flap being made of the skin and muscles at the side of the thorax this being filled with water before puncturing the intercostal spaces A third method is to dissect carefully through an intercostal space down to the pleura, when the lung will be found to be retracted On opening the thorax the appearances vary If the air entering the pleura is sterile no inflammatory reaction occurs the pleura

remains shiny and no fluid is formed, the condition being one of simple pneumothorax If bacteria have gained access to the pleura with the ingoing air or subsequently through the opening when this remains patent either serous fluid or pus collects In the former case the condition is described as hydro pneumothorax in the latter as pyo pneumothorax The appearances of the pleural membrane are similar to those found in serofibrinous pleurisy and empyema respectively The lung is collapsed in every case of pneumothorax, and lies retracted towards the hilum and the spine In tuberculous disease, a caseous focus or small cavity just under the pleura is the most frequent cause The perforation may be a large circular rent or a small pin hole, but multiple apertures may occasionally be present The opening can usually be found, even if small by submerging the lung under water while pumping air down the trachea When extensive adhesions are present, the collapse of the lung is largely prevented and the pneumothorax is only partial In such cases the perforation is frequently near the adhesions In cases where fluid is present the diaphragm may be seen to be depressed on the affected side and its curvature lessened or reversed

Symptoms —In a considerable proportion of cases the onset is sudden and the condition of the patient becomes alarming at once On the other hand pneumothorax may develop insidiously, with surprisingly little pain and dyspnœa, so that its occurrence may be overlooked or only discovered on routine physical and radiographic examination, including a lateral film This is more likely to be the case when perforation occurs in a lung extensively diseased or when the aperture is small and the leak of air is slow In the acute form of onset the patient is seized with severe pain while coughing or engaged in some extra exertion There is often a feeling of something having given way , and at once great dyspnœa develops with signs of collapse and severe mental anguish The patient may appear blue cold and clammy breathing is rapid and shallow the temperature falls to subnormal, the heart beats quickly and the pulse becomes small and weak The patient is often restless very alarmed and unable or afraid to speak Occasionally death occurs in a few minutes As a rule, the more acute symptoms subside in a few hours but the temperature rises and the rapid breathing usually persists for some time On examination the patient will usually be found sitting up, with alæ nasi working and with rapid shallow breathing The affected side is almost or entirely immobile and is usually bulged The displacement of the cardiac impulse towards the unaffected side is generally obvious, and is almost immediate Palpation confirms the absence of movement, and vocal fremitus is found to be absent, except where the collapsed lung remains in contact with the chest wall, over which area it may be increased The exact position of the cardiac impulse should also be determined in right sided cases it will be found in the left axillary region, in left sided cases it may be under or beyond the right nipple The liver may be felt much depressed in right sided cases The note over a pneumothorax is characteristically tympanitic or drum like as a rule but in cases with positive pressure the tympany may be flat and muffled The tympanitic area should be carefully mapped out, it may be found to extend across the middle line, or to encroach on or obliterate the liver dullness in right sided cases On the other hand in partial pneumothorax, the area may be small and easily escape recognition In left sided cases the cardiac dullness may be completely wanting on that side, and a dull area found to the right of the sternum This may give a useful hint as to the diagnosis On auscultation the breath sounds are often absent but they may be present at the apex, although weak In other instances distant tubular breathing may be audible from the collapsed lung in cases with a large patent opening hollow cavernous breathing may be heard The voice sounds have an amphoric or metallic quality, and an amphoric echo may occur with any sound produced near the pneumothorax Metallic tinkling is an example of this, being the quality conveyed to râles or other adventitious sounds produced in breathing The bell sound or *bruit d airain* is a

valuable sign but is not invariably present It is elicited by listening to the chest near where a coin is placed flat on it and tapped with another Where the acoustic conditions are right for the production of these musical sounds all sounds which produce rhythmic vibrations in the pneumothorax cavity will have a ringing quality whether they are rales voice sounds breath sounds coin sounds or even heart sounds The displacement of the heart can be confirmed by auscultation and the heart sounds may be found to have a metallic character When air and fluid are present in the pleura the signs are somewhat modified There is dullness at the base which shifts its level with the patient s movements the upper limit being straight in contrast with the curved line of ordinary effusions A marked succussion splash may be heard and felt on shaking the patient or the patient may demonstrate the sign by a sudden shake or jerk

Complications and Sequelæ—Cardiac failure and rapid death occur occasionally The chief complications are due to the entry of infective organisms into the pleura leading to pleurisy and the effusion of sero fibrinous fluid or pus The sequelæ may be pleural adhesions in cases that recover especially if effusion occurs There may be also permanent collapse of the lung in long standing cases, and in pyo pneumothorax a fistula either pleuropulmonary or external may remain in spite of treatment

Diagnosis—The recognition of a large or of a complete pneumothorax is easy as a rule the signs being characteristic When a large quantity of fluid is present in an open pneumothorax the presence of air may not be recognised until after paracentesis and radiographic examination The latter gives information of the greatest value and sometimes demonstrates the presence of local pneumothorax where it has not been suspected The air space between the lung and pleura shows most clearly in radiograms and if fluid is present as well the dead level of the upper border of the shadow varying with position is most characteristic Diagnosis is more difficult in cases where pleural adhesions exist, or where the pneumothorax is small and localised Sometimes very careful positioning of the patient and very close scrutiny of the radiographic film may be necessary before the slight collapse can be seen The following conditions may give rise to difficulty and should be considered in doubtful cases (1) Total excavation of a lung or a large pulmonary cavity in either of which the note may be boxy or even tympanitic the breath sounds amphoric and the rales metallic or tinkling while the coin sound may be obtained These conditions can usually be distinguished by the flattening and retraction of the chest wall over them and the absence of cardiac displacement or if it exists the traction of the heart towards the affected side by fibrosis (2) Advanced emphysema with complete obliteration of the cardiac dullness may be confused with pneumothorax. Large bilateral bullæ may be mistaken for bilateral pneumothorax (3) Massive collapse of one lung with compensatory emphysema of the opposite side may also be mistaken for it. In both these conditions careful examination will establish the real nature (4) A subphrenic abscess containing gas (subphrenic pyo pneumothorax), in this condition the diaphragm may be displaced upwards and the note over the lower ribs may be markedly tympanitic These signs are more suggestive when right sided Succussion splash and bell sound may be elicited The heart, if displaced is pushed upwards The history of previous abdominal disease may be helpful and a radiogram may give conclusive evidence of the subphrenic origin of the condition (5) A hernia of the stomach or bowel through the diaphragm or eventration of the diaphragm all rare conditions may simulate pneumothorax but in all there is generally abdominal flattening and little if any cardiac displacement A barium meal examination will as a rule establish the nature of the condition

Course and Prognosis—The course and prognosis of pneumothorax are profoundly influenced by the cause In cases due to rupture of an emphysematous vesicle or of a small localised healed tuberculous focus where the pleura remains sterile and the aperture of entry closes the air is usually completely absorbed in a

remains shiny and no fluid is formed, the condition being one of simple pneumothorax If bacteria have gained access to the pleura with the ingoing air or subsequently through the opening when this remains patent either serous fluid or pus collects In the former case the condition is described as hydro pneumothorax, in the latter as pyo pneumothorax The appearances of the pleural membrane are similar to those found in serofibrinous pleurisy and empyema respectively The lung is collapsed in every case of pneumothorax, and lies retracted towards the hilum and the spine In tuberculous disease a caseous focus or small cavity just under the pleura is the most frequent cause The perforation may be a large circular rent or a small pin hole, but multiple apertures may occasionally be present The opening can usually be found, even if small, by submerging the lung under water while pumping air down the trachea When extensive adhesions are present, the collapse of the lung is largely prevented and the pneumothorax is only partial In such cases the perforation is frequently near the adhesions In cases where fluid is present the diaphragm may be seen to be depressed on the affected side and its curvature lessened or reversed

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the adjacent tissue Contrary to what might be expected extensive pleurisy is uncommon until rupture or suppuration of the cyst occurs The pressure of the cyst may lead to collapse of the contiguous areas of lung and to displacement of the heart and mediastinum

Symptoms —These may be absent until the cyst is large enough to produce pressure symptoms such as dyspnœa pain and cough There is little or no expectoration unless rupture into a bronchus occurs when cyst wall daughter cysts and hooklets may be found in it There is no fever until suppuration occurs The signs are practically identical with those of encysted pleural effusion

Complications and Sequelæ.—Rupture and suppuration are the two most important complications Rupture may take place into the lung into the pleural cavity rarely through the chest wall or through the diaphragm At the time of rupture an urticarial rash may develop This is probably an anaphylactic phenomenon associated with the liberation of toxin present in the fluid of the cyst

Diagnosis —The symptoms and signs generally suggest either pleural effusion or new growth and hydatid disease may not be suspected Obscure basic signs in patients coming from countries where hydatid disease is common should suggest special methods of investigation as to the possibility of its presence Should it be suspected aspiration is to be deprecated unless all preparations for immediate operation are complete if the diagnosis is confirmed These methods comprise radiographic examination an eosinophil count the complement fixation test, the Casoni intra dermal test and the precipitin reaction (see p 325)

Course —The cyst may be latent for some time but it usually enlarges and produces increasing symptoms culminating in rupture or suppuration Very rarely death of the cyst occurs and its contents become inspissated

Prognosis —If untreated until rupture occurs a fatal result is most probable If diagnosed and treated before rupture the prognosis is not unfavourable

Treatment.—The former practice of aspiration and injection with formalin or iodine although sometimes successful is dangerous and should be discarded Exposure of the cyst by thoracotomy and its removal entire should be the treatment if practicable or if too large it may be aspirated and then dissected out.

ACTINOMYCOSIS OF THE PLEURA

The special features of the pulmonary localisations have been described It is possible although improbable that the infection may be primarily pleural Commonly clinical manifestations point to a predominating involvement of the pleura although the primary lesions may be in adjacent structures such as the lungs mediastinum or liver

Symptoms —The symptoms and signs in such cases are those of empyema but the following points are noteworthy The empyema is rarely large and it commonly extends through the chest wall producing a local swelling which soon discharges through the skin if untreated causing a suggestive infiltration and puckering around Exploratory puncture of an actinomycotic empyema often fails since the grumous caseous material it contains may be too thick to pass through the needle

Diagnosis —The characteristic sulphur granules in the pus may draw attention to the real nature of the condition but they are not always present Direct films should always be made from the pus obtained from empyemata The streptothrix may be found in this way when culture fails If the lung is involved as well as the pleura the organism may be found in the expectoration and the nature of the pleural condition may thus be established before operation

Prognosis —Some cases respond to treatment but prognosis is in general unfavourable death resulting from exhaustion or toxæmia due to dissemination of the disease

few weeks and recovery is often complete In tuberculous cases with extensive disease, the pleura becomes infected and death usually results in a few weeks or months although with judicious treatment life may be prolonged for years in some cases especially where surgical treatment such as thoracoplasty becomes practicable In pneumothorax secondary to some grave disease such as carcinoma or gangrene the course is brief and the prognosis is grave in the extreme In cases secondary to empyema surgical treatment may be followed by complete recovery

Treatment—In the majority of cases no treatment is required other than a few day s rest, with radiological control

In rare cases of pressure pneumothorax where the distress and dyspnœa are desperate no time must be lost in putting a needle into the pleural cavity to relieve the positive pressure Any wide-bore needle will serve in an emergency but a pneumothorax induction needle attached to a tube led off to a bottle on the floor under a water seal is better As soon as possible, however the pressure should be controlled with a pneumothorax apparatus and manometer, as in some cases the dyspnœa is not relieved until a negative pressure is achieved Severe dyspnœa must not be allowed for a second longer than necessary or death may follow swiftly even after the positive pressure has been relieved Morphine should not be given to these patients until their dyspnœa has been relieved In less urgent cases where there is no suggestion of a pressure pneumothorax, gr $\frac{1}{6}$ of morphine will help to reassure a somewhat alarmed patient If the pneumothorax is a large one and there is any distress the pressure should be taken and some of the air aspirated leaving a pressure slightly below atmospheric It is best to leave small pneumothoraces untapped and in any case except in the case of valvular pneumothorax it is unwise to remove too much air since the perforation in a partially collapsed lung is more likely to heal over than in an expanded one

In cases of recurrent spontaneous pneumothorax pleurodesis by the introduction of an irritant fluid may be necessary a 10 per cent solution of silver nitrate is often used, the quantity varying from 5 to 10 minims The treatment is often painful and may be followed by excessive pleural thickening It is rarely necessary If serous fluid or pus collects in the pleura it may be withdrawn preferably by siphonage and in this case, as also with removal of air, too much should not be withdrawn in the early stages as a slight positive pressure may assist in closure of the aperture in the lung whereas a negative pressure may open it, after it has begun to close

The question of operation in pneumothorax may be difficult to decide In cases secondary to empyema resection of a part of a rib and drainage often lead to satisfactory results In cases of moderately severe or advanced tuberculosis with pyopneumothorax open operation is generally contraindicated, and if performed is liable to result in a permanently open pneumothorax It is prefereable to remove fluid from time to time by aspiration with or without air replacement until thoracoplasty can be considered Penicillin or streptomycin may be injected into the pleural cavity as for empyema Surgical methods sometimes employed are intercostal tube drainage with slight suction water sealed drainage or thoracoplasty in several stages In pneumothoraces secondary to cystic disease of the lung lobectomy may be necessary

HYDATID DISEASE OF THE PLEURA

Hydatid cysts may be primary in the pleura or may encroach on the pleura, although originating in adjacent structures such as the lung liver, spleen or mediastinum (parapleural hydatid)

Ætiology and Pathology—Primary pleural hydatid is rare but secondary invasion of the pleura is more common In this situation the cyst may reach a large size even 5 or 6 in in diameter before rupture occurs As in other situations a fibrous capsule is developed around the cyst from the irritative changes set up in

expectoration often blood stained or it may involve the chest wall Metastases sometimes develop along the course of the needle track after aspiration of the fluid The secondary growths especially those in the glands, may exert pressure, *e g* the axillary glands may cause œdema and swelling of the arm A primary growth of the pleura may cause intense pain as it may split the costal cartilage from the sternum and invade the periosteum

Diagnosis—A chronic pleural effusion in a middle aged man, not associated with fever and not due to tuberculosis should arouse suspicion of malignant disease of the lung and pleura Evidence of fluid in one pleura at an interval after excision of the breast for malignant disease is very suggestive of secondary pleural growth A hæmorrhagic effusion not due to tuberculosis or renal disease should also arouse suspicion of malignancy, especially if reaccumulation after tapping is rapid and if the subsequent tappings show increasingly hæmorrhagic characters When aspiration of a considerable quantity of fluid gives little relief to symptoms, or when irregular dull areas remain where resonance might be expected the probability of growth must be borne in mind Growth involving the chest wall or the presence of cervical or axillary glandular metastases render it certain Radiological examination after removal of some of the fluid may show characteristic plaques on the pleura

Course—This is almost invariably progressive, the duration being rarely more than 2 years and occasionally much less

Prognosis—Malignant growth of the pleura is invariably fatal unless removal is possible

Treatment—From the nature of the condition this can only be palliative Analgesic drugs may be given freely for the relief of pain morphine being reserved for the severe forms and later stages as far as possible Repeated tappings may be almost compulsory if there is much distress from the reaccumulation of the fluid but it must be remembered that in hæmorrhagic effusions the loss of blood by this means is considerable Air replacement may sometimes give relief for a longer period than simple aspiration In rare cases removal by operation may be practicable if the diagnosis is made early and the growth is localised in an accessible position Deep X ray therapy may relieve the pain

INJURY

Injury to the pleura may occur in fracture of the ribs, the fragments piercing or tearing it Similarly in penetrating wounds of the chest the pleura may be extensively lacerated It may also be torn by direct violence without breaking of the ribs and in rare cases a hernial protrusion of lung may occur forming a small swelling in an intercostal space protruding with inspiration and emptying with expiration

R A Young
G E Beaumont
E R Boland

DISEASES OF THE DIAPHRAGM

SPASM OF THE DIAPHRAGM

Diaphragmatic spasm may be either clonic or tonic the former being termed *hiccough*

Clonic spasm—This may be due to a variety or causes namely (*a*) Alimentary

Treatment—(See p 196) The pultaceous pleural contents should be removed as far as possible by operation Penicillin should be given as for actinomycosis of the lung and injected intrapleurally

SIMPLE TUMOURS OF THE PLEURA

These are very rare and are as a rule only discovered after death They are almost invariably of extrapleural origin and their presence in the pleura is due to the direction taken by the growth Lipoma of the subpleural or of the mediastinal fat may occur as small pedunculated tumours or very rarely as a large mass They can be differentiated from tumours of the lung by radiographic examination after a diagnostic pneumothorax

MALIGNANT TUMOURS OF THE PLEURA

Primary malignant disease of the pleura is rare, and may take the form of endothelioma carcinoma or sarcoma Secondary carcinoma and sarcoma are more common

Ætiology—*Primary endothelioma of the pleura is more common* in late adult life and in the male sex Sarcoma is more likely to occur in children and in young adults Secondary growths may occur at any age but more commonly in later life

Pathology—Endothelioma of the pleura is a growth of obscure origin It has not been conclusively established that it is derived from the pleural endothelial cells and by some writers it is classed as a carcinoma It is at first unilateral but it involves the affected pleura over a wide area sometimes universally The membrane appears to be overlaid with an irregular rough hard covering sometimes nodular In other cases there is more thickening and the condition may be localised There is nearly always a large amount of blood stained serous effusion The condition may spread to the bronchial or supraclavicular glands the lung, the spine the diaphragm and the peritoneum

Primary carcinoma of the pleura has also been described but is very rare Primary sarcoma is also extremely uncommon but the round celled and spindle celled varieties may occur and angio sarcoma, fibro sarcoma myxo sarcoma and chondro sarcoma have all been recorded

Secondary carcinoma and sarcoma of the pleura are relatively *common* and may occur from direct *extension* in growths of the lung bronchi and mediastinum by *metastases* of growths in almost any distant part or by *lymphatic permeation* in mammary carcinoma *In the last named condition pleural and pulmonary growths* are a not infrequent form of recurrence sometimes occurring months or years after removal of the primary growth

Symptoms—These are not characteristic and increasing dyspnœa due to an accumulation of fluid may be the first indication More commonly pain and cough similar to those of pleurisy may occur acutely or develop more gradually Although afebrile as a rule the occurrence of fever does not exclude malignant disease Cachexia and wasting are often not marked until the condition is advanced The signs are generally indistinguishable from those of ordinary pleural effusion unless secondary growths become manifest in the cervical or axillary glands Sometimes coarse dry friction may be heard, or there may be signs of pleural thickening *without fluid* There is often local pain and tenderness over the chest Exploratory puncture may demonstrate the hæmorrhagic character of the effusion *The specific gravity* is generally 1·018 or over and *the cytology of the fluid may be suggestive* especially if excess of endothelial cells often aggregated into plaques is found

Complications—The growth may spread to the lung and cause cough and

expectoration often blood stained or it may involve the chest wall Metastases sometimes develop along the course of the needle track after aspiration of the fluid The secondary growths especially those in the glands, may exert pressure *e g* the axillary glands may cause œdema and swelling of the arm. A primary growth of the pleura may cause intense pain as it may split the costal cartilage from the sternum and invade the periosteum

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Diaphragmatic spasm may be either clonic or tonic the former being termed *hiccough*

Clonic spasm —This may be due to a variety or causes namely (*a*) Alimentary

from irritation of the œsophagus or stomach by pungent or irritant substances such as pepper, pickles or tobacco It occurs also as a symptom in gastritis dilatation of the stomach enteritis intestinal obstruction tympanites and peritonitis, and in the late stages of debilitating disease (*b*) Nervous as in hysteria, cerebral tumour meningitis hydrocephalus epilepsy and alcoholism It may also result from peripheral nerve irritation in such conditions as mediastinal tumour mediastinitis enlarged thoracic glands, diaphragmatic pleurisy or pericardial effusion During epidemics of encephalitis lethargica hiccough has occurred as a symptom There is usually some slight pyrexia and the condition may persist without intermission for several days (*c*) Renal as in chronic nephritis and uræmia

Tonic spasm —This may be met with in tetanus strychnine poisoning laryngismus stridulus, eclampsia, epilepsy and hydrophobia If there is associated intercostal or laryngeal spasm there is grave risk of death from asphyxia

Treatment —Simple hiccough may often be relieved by holding the breath pressure on the chest or by simple inhalations such as of ammonia ether or spirits of chloroform Hiccough due to organic disease or to peripheral irritation may only be relieved by removal of the cause In epidemic hiccough, in obstinate cases of hiccough due to other causes and in the tonic form of spasm various antispasmodic measures may be tried such as trinitrin bromides or phenobarbitone by the mouth adrenaline or adrenaline and pituitary (posterior lobe) extract, hypodermically, or the inhalation of chloroform In some cases relief may be obtained by spraying the skin above the clavicle with ethyl chloride Injection of the phrenic nerve with procaine has been used with success when all other methods have failed

DIAPHRAGMATIC PLEURISY

This condition is described on p 1065 under the heading of Pleurisy

PARALYSIS OF THE DIAPHRAGM

Definition —Paralysis and inactivity of either leaf of the diaphragm or of both

Ætiology —Paralysis of the diaphragm may be caused by disease damaging the centre in the spinal cord by conditions affecting the phrenic nerve in its course or by reflex inhibition of the centre Causes involving the centre include poliomyelitis hæmorrhage into the spinal cord and tumours of the spinal cord or its membranes or of the spine itself The phrenic nerves may be affected by diphtheritic neuritis Either or both of the nerves may be compressed by mediastinal tumours or by inflammatory exudates They may be severed or injured by wounds in the neck Evulsion or crushing of the phrenic nerve is now frequently employed therapeutically, in order to promote collapse of the base of one lung and closure of cavities in cases of tuberculosis and in bronchiectasis Occasionally no cause for the paralysis may be found

Symptoms —Diaphragmatic paralysis results in the affected leaf of the diaphragm becoming immobile and remaining at a higher level in the thorax than normal or showing paradoxical movement *i e* ascending with inspiration This can easily be seen on radiographic examination Sometimes this is noted as a reversal of the ordinary abdominal movements during respiration with the result that there is epigastric recession during inspiration In elderly patients the diaphragmatic paralysis sometimes causes dyspnœa on exertion and some discomfort after meals

Treatment —This is in general, that of the condition causing the paralysis

EVENTRATION OF THE DIAPHRAGM (see p 647)

DISEASES OF THE MEDIASTINUM

The mediastinum is the interpleural space and occupies the median part of the thorax from the superior aperture above to the diaphragm below Strictly speaking any affection of any of the important structures occupying this space such as the pericardium heart great vessels air passages and the thymus might be included under this heading They are however more conveniently grouped under the various systems to which they belong and diseases of the mediastinum are commonly restricted to conditions arising in or affecting the connective tissue and glands found in this space

MEDIASTINITIS

Mediastinitis or inflammation in the mediastinal connective tissue may be acute or chronic In the acute forms there may be an inflammatory serous exudate causing œdema or the inflammation may progress to abscess formation The chronic forms are indurative or fibroid in character although chronic abscess may occur

ACUTE SIMPLE MEDIASTINITIS

Ætiology—Acute mediastinitis without suppuration may result from injuries to the chest wall or sternum, and from lacerating wounds of the œsophagus or trachea It is sometimes secondary to inflammatory processes in the lungs pleuræ, pericardium or peritoneum and to periostitis of the sternum or vertebræ Pneumonia is a not uncommon cause

Pathology—There is a hyperæmia of the mediastinal connective tissue with inflammatory œdema Mediastinal serous effusions have been described but these are without doubt encysted pleural effusions encroaching on the mediastinum

Symptoms—The clinical manifestations of acute mediastinitis are vague and not characteristic There is a mild pyrexia the temperature reaching 99 or 100° F Pain under the sternum may be complained of, and on auscultation over it a few fine crepitations *may be heard on deep breathing or they may occur synchronously with* the heart beats

Diagnosis—Mediastinitis is often not recognised or suspected since it is masked or overshadowed by the clinical manifestations of the primary condition

Course—The affection may subside or proceed to abscess formation It may result in fibroid thickening or adhesions

Treatment—No special treatment is required, apart from that appropriate to the condition inducing it

ACUTE SUPPURATIVE MEDIASTINITIS

Ætiology—Acute suppurative mediastinitis or mediastinal abscess is more common in males and may occur at any age although it is more frequently seen in early adult life than at other periods Some cases are of traumatic origin and follow perforating wounds or blows on the sternum not necessarily causing fracture Perforation or injury of the œsophagus is a comparatively frequent mode of access of pyogenic organisms to the mediastinum This may occur from ulceration of an œsophageal new growth from injury due to a swallowed body such as a tooth plate, or from the passage of an œsophagoscope or bougie Perforation of the trachea or main bronchi by an inhaled foreign body is sometimes the cause of *mediastinal suppuration* Various

pulmonary conditions may lead to pyogenic infection of the mediastinum such as pulmonary abscess or gangrene pneumonia and bronchiectasis Periostitis or osteomyelitis of the sternum, vertebræ or ribs suppuration in the mediastinal glands or tracking down of deep cervical abscesses may all lead to mediastinal abscess Extensions of pyogenic processes from the pericardium pleura or peritoneum may also be causes A suppurating hydatid or dermoid cyst may rupture into the mediastinum and lastly the infection is blood borne in some cases from infective endocarditis pyæmia erysipelas or enteric fever Dieulafoy pointed out that certain cases of empyema, originating near the mediastinum, may, by encroaching on this region induce predominating mediastinal symptoms, which he described as the 'mediastinal syndrome' Such cases although abscesses encroaching on the mediastinum are not mediastinal abscesses but are in reality special instances of encysted empyema

Pathology —The suppuration may be limited to any part of the anatomical subdivisions of the mediastinum or may spread from one compartment to another The pus sometimes tracks in various directions *e g* upwards to the neck downwards to the abdomen, or it may point in the chest wall The abscess may rupture into the œsophagus trachea aorta pleura or pericardium

Symptoms —The onset may be insidious or acute In the latter case it may be ushered in by severe pain under the sternum, radiating to the back and shoulders The symptoms may be divided into those due to the inflammatory process and those resulting from the pressure exerted by the collection of pus The former comprise malaise fever and sometimes rigors while blood examination may demonstrate a leucocytosis of 10 000 per c mm or over The pressure symptoms vary according to the amount of pus produced and its situation They include dyspnœa and paroxysmal or brassy cough from compression of the vagus nerve or direct pressure on the trachea There may also be dysphagia from obstruction of the œsophagus and hoarseness from pressure on the left recurrent laryngeal nerve Pressure on the spinal nerve roots intercostal nerves or brachial plexus may lead to severe neuralgic pains Partial or complete obstruction of the great veins may be apparent from distension of the superficial thoracic veins or of those in the neck Oedema of the chest wall is sometimes seen from this cause or it may result from the inflammatory process extending to the chest wall The signs in severe cases will be those caused by the pressure effects just described The patient looks ill distressed dyspnœic and more or less cyanosed The respirations may be noisy as there is sometimes inspiratory dyspnœa with stridor, this being known as the *bruit de cornage* The dilated veins may be apparent and the direction of the current may help to localise the seat of the obstruction There is sometimes local redness and œdema from pointing of the abscess near the sternum in the neck or in the interscapular region on either side Palpation may reveal local tenderness and even fluctuation in any of these areas There is often dullness over the sternum sometimes extending to one or other side or the dullness may be found in the interscapular region It is said that the dullness may shift with the position of the patient in some cases Breath sounds are distant and weak or bronchial over the dull area except when it is behind the sternum when they are harsh

Complications and Sequelæ —The important complications are those due to rupture of the abscess If this occurs into the lung or the œsophagus pus is expectorated, or passes into the stomach Gangrene of the mediastinum may follow, or death may occur from suffocation or hæmorrhage Extension of the abscess may lead to purulent pleurisy, pericarditis or peritonitis or to suppuration in the neck In cases that recover, chronic mediastinitis with matting together of the mediastinal contents may be a sequel

Diagnosis —The mediastinal syndrome of dyspnœa stridor paroxysmal cough hoarseness and dysphagia with signs of pressure on arteries veins and nerves is common to many conditions causing mediastinal pressure notably mediastinal

new growth enlarged mediastinal glands aneurysm and pericardial effusion The differential diagnosis of these is more fully considered under mediastinal new growth The occurrence of fevers and rigors the presence of a pointing swelling and the demonstration of a leucocytosis may give strong suggestion as to the inflammatory origin of these symptoms and signs The radiograph may reveal a localised mediastinal shadow often non pulsating although it must be remembered that in rare cases a mediastinal abscess may pulsate

Course —The disease is acute and rapidly progressive unless relieved by operation or by spontaneous external drainage in a few fortunate cases

Prognosis —This is very grave and the majority of cases die unless recognised and treated early If gangrene develops a fatal result is inevitable The outlook is more hopeful when the anterior mediastinum alone is involved

Treatment —PROPHYLACTIC —Foreign bodies in the œsophagus and trachea should be removed as soon and as gently as possible The utmost care should be exercised in the passage of a bougie or the œsophagoscope in cases of œsophageal stricture

CURATIVE —As soon as mediastinal suppuration has been diagnosed and localised surgical measures should be adopted The mediastinum can be reached by resection of pieces of costal cartilage or by trephining the sternum appropriate antibiotic treatment should be given

CHRONIC MEDIASTINITIS

This also occurs in two forms chronic indurative mediastinitis and chronic abscess

CHRONIC INDURATIVE MEDIASTINITIS —This may occur as a sequel of any form of acute mediastinitis The best known is that associated with chronic adhesive pericarditis and usually known as chronic indurative mediastino pericarditis (pp 77 883) Other forms include the chronic inflammation and thickening which occur around enlarged sclerotic and pigmented mediastinal glands and around the same glands when affected by caseous or calcareous tuberculous lesions

CHRONIC MEDIASTINAL ABSCESS is generally of tuberculous origin arising from breaking down caseous bronchial or mediastinal glands or from tuberculous disease of the spine or ribs A chronic abscess may however be caused by a foreign body such as a bullet

Symptoms —Simple indurative mediastinitis may give rise to practically no symptoms or signs Chronic abscess may cause symptoms of ill health and of mediastinal pressure or may only become apparent when it points superficially

Treatment —The treatment of chronic mediastinal abscess is practically the same as that for other cold abscesses due to tuberculosis incision and drainage being avoided if possible in favour of aspiration and chemotherapy Other cases may require operation

EMPHYSEMA OF THE MEDIASTINUM

In performing tracheotomy the pretracheal layer of deep cervical fascia is of necessity incised If difficulty arises in inserting the tube into the tracheal incision air may be drawn deep to this fascia by the vigorous attempts at respiration and thus pass into the superior mediastinum or superficial to it into the anterior mediastinum Rupture of the trachea bronchi or œsophagus or rupture of air vesicles or pulmonary lesions where the pleura is adherent may also cause it In acute interstitial emphysema of the lungs the escaped air may track along to the root and reach the mediastinum

Symptoms —Emphysema of the *mediastinum may give rise to very indefinite*

indications A few fine crackling sounds may be heard on listening over the sternum sometimes varying with respiration or with the heart movements The percussion note over the praecordium may be hyper resonant, and the heart sounds may be distant and muffled Small quantities of air escaped into the mediastinum can be rapidly absorbed and may not be of serious import

Diagnosis —This is often a matter of speculation, unless the air spreads upwards to the neck and causes superficial surgical emphysema

Prognosis —This depends entirely on that of the underlying cause, which is often of serious nature

Treatment —No special treatment is required, as a rule, apart from that of the primary condition except that pain may necessitate the use of analgesic drugs at the onset

ENLARGED MEDIASTINAL GLANDS

The mediastinal lymphatic glands are arranged in groups A few small ones are found in the anterior compartment another group is situated in the posterior mediastinum The most important of these is the tracheo bronchial group situated around the bifurcation of the trachea and extending along the bronchi It is enlargement of this group that most often gives clinical manifestations

Ætiology and Pathology —A simple inflammatory enlargement of these glands may occur in many acute affections of the bronchi and lungs and in certain acute specific fevers notably influenza pertussis and measles A more chronic enlargement associated with indurative changes results from chronic respiratory diseases such as chronic bronchitis and the pneumoconioses In the latter case, considerable pigmentary changes may be found from deposition of the particles derived from the dusty inspired air In town dwellers, these glands are often grey or black in colour from deposited carbon Tuberculosis is the commonest cause of enlargement of the mediastinal glands particularly of the tracheo bronchial group those about the right bronchus being most affected as a rule This is a frequent early localisation of tuberculous disease in children The infection spreads from the lungs in the majority of cases (Ghon) but in some instances the path of infection is from the tonsils through the cervical lymphatics and glands while in others the mode of entrance is from the intestines through the mesenteric glands The lesions may be miliary tubercles or small caseous nodules which calcify subsequently, or which may soften and lead to local spread or generalisation In other cases a fibroid hyperplasia of the gland results

Enlargement of the mediastinal glands due to sarcoidosis is now realised to be a common condition as a result of routine radiography It is often asymptomatic

In syphilis mediastinal adenitis may occur in the secondary or tertiary stages In Hodgkin s disease and in lymphatic leukæmia the mediastinal glands may share in the general adenopathy and in the former the condition may be primary in these glands Enlargement due to malignant disease is of great importance and receives separate consideration

Symptoms —These may be slight and escape notice unless the enlargement is sufficient to produce pressure or irritation Cough is the commonest symptom it is usually dry irritative noisy and ineffective It may occur in paroxysms somewhat suggestive of those of whooping cough Dyspnœa and dysphagia occur only when the enlargement is considerable Vomiting sometimes develops probably reflexly from vagal stimulation Pain behind the sternum or in the upper thoracic region posteriorly may be complained of In children with tuberculous disease in these glands there is often languor anorexia anæmia and wasting sometimes with slight irregular fever and night sweats Such symptoms in a child of 5 to 12 years of age are very suggestive The signs are also variable and frequently inconclusive

In glandular enlargement from any cause, there may be dilated veins over the front or back of the chest especially in the upper part, and a hilum dimple has been described as appearing in the second intercostal space beside the sternum on holding the breath at the end of inspiration One pupil may be larger than the other owing to sympathetic stimulation Small areas of dullness may be found at the back near the upper thoracic spines or in front close to the manubrium Breath sounds over these areas may be bronchial or harsh Occasionally the enlarged glands impede the air entry to a lower lobe generally the right in which case breath sounds are notably weakened over this area while the percussion note may be impaired Normally whispering pectoriloquy ceases at the seventh cervical spine with enlarged mediastinal glands it may be heard along the middle line or close beside it in the upper thoracic region from the first to the fifth thoracic spines This is known as d Espine s sign or tracheophony It is a confirmatory sign when other indications are present Eustace Smith s sign is of little value It consists in a venous hum audible over the manubrium sterni when the child s head is thrown back as far as possible Most of these physical signs are of historical interest only as diagnosis is unreliable without radiological information Occasionally pressure on the recurrent laryngeal nerve may lead to an abductor paralysis of one vocal cord In cases of tuberculosis syphilis Hodgkin s disease or leukæmia enlarged glands may be present in other parts of the body and may thus assist in diagnosis

Complications—A caseous gland may ulcerate into a bronchus or into the trachea and death has resulted from glottic impaction of a portion of the gland Ulceration into the œsophagus has been described Rupture into the mediastinum may lead to mediastinal abscess Invasion of the pleura lung or pericardium may occur or generalisation causing widespread miliary tuberculosis Compression by tuberculous glands may lead to lobar collapse and bronchiectasis may follow

Diagnosis—Whenever the condition of mediastinal glandular enlargement is suspected radiographic examination should be made if possible It may help to distinguish between other conditions causing mediastinal pressure such as aneurysm abscess and malignant growth Unfortunately in tuberculous disease it shows best the condition of least importance namely the old healed calcified glands The Mantoux test should be used to differentiate between tuberculosis and sarcoidosis

Prognosis—This varies with the cause being serious in Hodgkin s disease and leukæmia In tuberculous cases the prognosis is as a rule good apart from complications provided treatment is prompt and adequate The prognosis of this form of sarcoidosis is excellent

Treatment—In tuberculous adenitis the general condition should be improved by every possible means The child should be taken from school rest and exercise are to be carefully graduated and a liberal diet supplied with extra milk cream and butter Cod liver oil and malt extracts are useful In glandular enlargements due to syphilis Hodgkin s disease and leukæmia the treatment appropriate to these diseases should be employed and symptoms due to pressure relieved as far as possible Opinions differ as to whether tuberculous adenitis and the primary lesion which gives rise to it should be treated with antibiotics Undoubtedly most cases recover without but treatment with streptomycin and isoniazid should be given in very young children or where there are complications such as bronchial ulceration or compression or any suggestion of post primary spread or where the severity of symptoms suggest any doubt as to the usually favourable outcome

MEDIASTINAL TUMOURS OR NEW GROWTHS

Routine radiology and thoracic surgery have enlarged our knowledge of mediastinal tumours

NEUROGENIC TUMOURS divided into neurofibromata and ganglio neuromata are

found mainly in the posterior mediastinum Simple tumours often reach a considerable size before giving rise to any symptoms but about 15 per cent undergo malignant changes Occasionally they are associated with von Recklinghausen s neurofibromatosis

DERMOIDS and TERATOMATA are congenital cysts which are usually found in the anterior mediastinum They often give rise to no symptoms but they have a definite tendency towards malignant change

LYMPHOBLASTOMA and LYMPHOSARCOMA produce considerable mediastinal enlargement with pressure symptoms They are usually very sensitive to radiotherapy and their disappearance *after a few exposures is almost diagnostic, but they soon* recur and eventually fail to respond to radiotherapy

LYMPHADENOMA or HODGKIN S DISEASE causes mediastinal tumours similar to *those of lymphosarcoma They also respond to radiotherapy but not quite so quickly* or completely, although the effect often lasts longer

THYMOMA —This tumour is found usually in the anterior and upper part of the *chest but they may occur over the pericardium or even on a level with the diaphragm* Their presence is sometimes associated with myasthenia gravis and they sometimes become malignant

INTRATHORACIC GOITRE —Colloid goitre sometimes descends into the anterior mediastinum behind the upper end of the sternum where it may cause pressure symptoms It can sometimes be felt from above on deep inspiration or during swallowing and it often causes deviation of the trachea with respiratory symptoms

PLEURO PERICARDIAL CYSTS are simple cysts lined by flattened epithelial cells and filled with a clear colourless liquid from which they get the name Spring water cysts In origin they are congenital arising from the pleural cavity at the 15 mm embryonic stage They are found lying in the cardio phrenic angle usually on the right side, and may be circular or lobulated in outline They seldom give rise to any symptoms unless they become very large This is unusual and their chief importance clinically is due to the errors in diagnosis that may arise when they are seen in a radiograph of the chest

MEDIASTINAL GLANDS may become very massive in bronchial carcinoma so that they overshadow the primary lesion and in primary tuberculosis in children and non immune native races they may give rise to mediastinal symptoms

HYDATID CYSTS of the mediastinum are rare in this country although they arise in the more primitive agricultural countries of the Continent, the Americas and Australia

OTHER TUMOURS occasionally occur lipomata meningocele hæmangioma and chondromata are worthy of mention

Pathology —The morbid appearance depends upon the situation of origin the directions of growth and the nature of the tumour Sarcomata are generally soft pinkish in colour and vascular while carcinomata are paler and firmer There may be one large mass weighing several pounds or there may be multiple growths When the tumour reaches a considerable size it may infiltrate, surround compress or displace contiguous structures This is particularly the case in the lympho sarcomata The trachea œsophagus and large vessels may be surrounded the pericardium and heart may be extensively infiltrated and the nerve trunks may be enclosed and compressed Secondary deposits are common in other glands but not infrequently the pigmented bronchial glands may be seen entirely enclosed in growth without being infiltrated

Symptoms —The onset is often insidious and the condition may not be suspected until cachexia and pressure signs develop Malaise weakness shortness of breath cough and pain are often early symptoms which become more pronounced as the case progresses The pressure symptoms and signs constituting the mediastinal syndrome comprise—

1 *Pressure on the air passages* giving rise to dyspnœa cough and expectoration

The dyspnœa may be inspiratory and associated with stridor or expiratory and paroxysmal The cough is harsh and may be 'brassy', it is often associated with mucoid blood stained or even prune juice sputum Bronchiectasis may result in some cases

2 *Pressure on or infiltration of the lung* leading to collapse and sometimes breaking down of lung tissue If the pleura is reached or invaded pleural effusion often blood stained may result

3 *Pressure on arteries*—Compression of branches of the pulmonary artery may lead to local gangrene or in other cases the growth may ulcerate into a larger vessel and cause fatal hæmorrhage Pressure on the subclavian artery may cause inequality of the radial pulses and according to Ekgren this may only be present when the patient is lying and not when he is standing

4 *Pressure on veins*—Dilated tortuous veins may be seen over the front of the chest and abdomen or in the neck The flow of blood in these superficial veins may be reversed in direction owing to the obstruction of the superior vena cava or its main radicles The current then runs from above downwards instead of from below upwards as normally There may be œdema of the chest wall or of the face and neck from the same cause

5 *Pressure on nerves*—The vagus may be compressed causing paroxysmal dyspnœa and cough Laryngeal paralysis or spasm may result from involvement of the recurrent laryngeal nerve Dilatation of the pupil followed later by constriction drooping of the upper lid and enophthalmos occurs when the sympathetic is involved (Horner s syndrome) Paralysis of the diaphragm on one side from compression of the phrenic nerve and pain from involvement of the intercostal nerves may be present

6 *Pressure on the œsophagus* may lead to dysphagia of increasing degree

In addition to the signs afforded by these various conditions there may be glandular enlargements in the neck the suprasternal notch or in the axillæ The growth may invade the chest wall at any spot and in rare cases it may cause visible or palpable pulsation The pulmonary physical signs are dyspnœa sometimes orthopnœa and cyanosis In some instances the patient prefers to lean forward this is said to be due to the fact that in this position the antero posterior diameter of the mediastinum is increased and the tension caused by the growth is thereby lessened There may be dullness over the sternum or over the upper thoracic spines and over any part of the lung invaded or compressed by the growth The breath sounds heard over the dull area may be harsh bronchial tubular weak or absent. The signs due to any secondary condition such as bronchitis bronchiectasis or a pleural effusion may be found in addition

Complications—These include the secondary conditions just mentioned Others are due to ulceration of the growth through the chest wall or into the trachea bronchi œsophagus or aorta Pericarditis may occur if the growth invades the pericardium and hæmopericardium may result from ulceration of a vessel

Diagnosis—When signs of mediastinal pressure become apparent, new growth should be suspected in common with aneurysm mediastinal abscess or cyst enlarged mediastinal glands and pericardial effusion The history the general condition of the patient the physical signs blood examination and the radiograph may all help in distinguishing between these conditions The evidence afforded by the radiograph may be of the utmost value The pulsating shadow of an aneurysm the large area of a pericardial effusion the indefinite edge of an infiltrating growth extending into the lung may be shown clearly but the appearance should always be interpreted in the light of the other clinical features and a diagnosis should not be made on radiographic findings alone since a growth may pulsate or may give rise to an effusion while a mediastinal abscess or a cyst may give a sharp shadow An œsophageal new-growth can sometimes be differentiated by the œsophagoscope but this should only

be employed when aneurysm can be excluded Diagnosis from bronchial new growths may be almost impossible Before the onset of pressure symptoms, growth may be suspected from the cough and emaciation, and here again the radiograph may give valuable indications Chronic tuberculous disease should always be excluded by repeated sputum examinations The diagnosis of mediastinal growth may sometimes be obscured by some of the complications it induces, notably pleural effusion and bronchiectasis The rapid onset and progress of these conditions and the blood stained character of an effusion may all suggest the possibility of a malignant cause The presence of enlarged glands in the neck or axillæ or of nodular growth in the chest wall or episternal notch may afford almost conclusive evidence of malignancy

Course—Malignant growths enlarge and the course is often rapid, particularly in lympho sarcoma Fulminating cases lasting only a few weeks occur, more commonly the patients live from 6 months to 2 years from the onset rarely more Simple tumours often give rise to no symptoms and are discovered as a result of routine radiological examination

Treatment—Since simple tumours may grow in size and cause pressure symptoms or become malignant they are better removed if this is possible although if left they do not necessarily cause death or disability The treatment of inoperable malignant tumours is that of inoperable malignant disease elsewhere Deep X rays or radium treatment in some form may be tried Otherwise treatment is symptomatic and palliative Pain may be relieved by aspirin codeine or morphine Sleep may be induced if there is insomnia by chloral hydrate, papaveretum Omnopon) or other hypnotics If effusion is causing dyspnœa it may be tapped, but the fluid usually collects again rapidly

DIAPHRAGMATIC HERNIA

Definition—Protrusion of an abdominal viscus usually the stomach, through the diaphragm into the thorax

Ætiology—The condition may be congenital or acquired some of the latter being due to trauma or inflammatory necrosis The majority of cases result from a congenital defect in the development of the diaphragm Congenital herniæ are usually false, there being no covering sac as a portion of the diaphragm is missing They occur dorso laterally through the foramen of Bochdalek, posteriorly through the œsophageal hiatus or parasternally through the foramen of Morgagni The stomach omentum colon, small intestine liver duodenum pancreas cæcum or kidney may protrude into the thorax

The acquired variety when not due to trauma or necrosis constitutes the para œsophageal hernia A portion of the stomach passes through the œsophageal hiatus and being enclosed in a sac constitutes a true hernia This may be due to delay in descent of the stomach constituting a congenital short œsophagus so that the œsophageal gap around the cardiac end of the stomach is larger than that which normally occurs around the narrow lower end of the œsophagus The difference in pressure between the abdomen and thorax which is accentuated by muscular strain atrophy of the diaphragmatico œsophageal membrane which fixes the diaphragm to the lower end of the œsophagus and the cardiac end of the stomach and the fact that the œsophageal opening is lax so that it may distend when the œsophagus is filled with food are further factors which may lead to the development of a hiatus hernia Traumatic herniæ are due to wounds or crushing injuries of the thorax or abdomen which involve the diaphragm They are more common on the left side owing to the protection afforded by the liver on the right side Subphrenic abscess empyema or abdominal carcinoma may lead to inflammatory necrosis and herniation of the diaphragm The hiatus type of hernia is by far the most common clinically

Symptoms —The symptoms of congenital diaphragmatic hernia are dyspnœa cyanosis abdominal pain and distension and vomiting In many cases of hiatus hernia there are no symptoms the condition being revealed by barium meal examination In others the patient complains of dysphagia eructations hiccough abdominal pain vomiting or hæmatemesis Some of the symptoms are due to the ulceration which is sometimes found in the herniated viscus An otherwise inexplicable secondary anæmia may be due to bleeding from such a lesion

Diagnosis —The diagnosis is established by barium meal examination of the patient lying in the Trendelenberg position In some cases of hiatus hernia the symptoms may suggest disease of the gall bladder in others angina pectoris or organic lesions of the œsophagus may be simulated

Prognosis —Death often occurs in the congenital type within a few days of birth Better results are obtained by operation within 48 hours than by waiting for a week or 10 days In some series a 50 per cent cure has been obtained.

Treatment —Medical treatment consists in small and frequent feeds and avoidance of lying down shortly after a meal In the majority of cases giving rise to symptoms surgery is required various types of repair operation being performed according to the nature of the lesion

R A Young
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SECTION XIV

DISEASES OF THE KIDNEYS

THE CHARACTERS OF NORMAL URINE

NORMAL urine is a clear amber coloured fluid A slight gelatinous mucoid deposit, called the nubecula settles out of it on standing The quantity of urine secreted in 24 hours is about 50 oz or 1500 ml , it depends on the amount of food eaten and fluid drunk and on the amount of fluid lost by the skin lungs and bowel Solid food accounts for 33 to 50 per cent of the total fluid intake About 75 per cent. of the total intake is excreted by the kidneys but on any one day the variation may be 50 to 95 per cent of the intake The specific gravity usually varies between 1 015 and 1 025 Individual specimens may be 1 005 or less if much fluid has been drunk or 1 035 on a dry diet or as the result of much fluid being lost through the skin or bowel The concentration of chlorides and phosphates has more effect in raising the specific gravity than has urea The presence of glycosuria may make the specific gravity still higher The reaction is generally acid due to acid sodium phosphate. The total acidity is such that about 650 ml of decinormal caustic soda will neutralise the daily output but in acidosis the total acidity may be doubled even despite large doses of alkalis The *p*H of individual specimens varies between 4 7 and 10 Urine is more acid during fasting than during digestion while hydrochloric acid is being secreted in the gastric juice Protein food tends to make the urine acid, but fruit and vegetables tend to make it alkaline because the organic acids in these foods are converted into alkaline carbonates which are excreted in the urine It may be alkaline after rising in the morning due to increased activity of the respiratory centre the so called alkaline tide On decomposition either in the bladder or after evacuation the urine becomes alkaline from the conversion of urea into ammonium carbonate

The constituents of urine are partly derived from the food (exogenous) and partly from the katabolism of the tissues (endogenous) We may briefly consider the source and significance of the principal constituents

Nitrogenous constituents —The total nitrogen excreted each day on an ordinary mixed diet is about 18 grammes Of the various nitrogenous constituents urea is by far the most abundant its output being 33 g which contains 15 4 g of nitrogen or 85 per cent of the total nitrogen As so much of the urea comes directly from the food the amount of urea falls both absolutely and relatively in starvation the total nitrogen drops to 5 g or even less of which urea nitrogen forms about 60 per cent. On a diet rich in carbohydrates and fat but containing hardly any nitrogen these figures may fall still lower as the assimilation of other foodstuffs reduces the waste of tissue nitrogen to a minimum This is often forgotten and in nephritis undue importance is attached to a drop in the output of urea which is simply due to the diet prescribed being poor in nitrogen

The purine bodies are next in importance The best known is uric acid (tri oxy purine) A small quantity of the less oxidised purines xanthine and hypoxanthine is also excreted Uric acid is only excreted as such when the urine is concentrated and highly acid it normally appears as acid sodium urate (see Gout p 444)

Creatinine the anhydride of creatine is in some way related to muscle metabolism, 1 to 1 5 g are excreted daily It is unimportant in relation to kidney disease but endogenous (*i e* fasting) creatinine clearance roughly parallels inulin clearance and provides a relatively simple indication of glomerular filtration rate It is curious that the urine of the adult male contains no creatine or only traces of it whereas children

excrete both creatine and creatinine and in the female the excretion of creatine is intermittent It is however continuous in pregnancy

Ammonia is normally excreted to the extent of 0 5 to 1 g daily The kidney conserves plasma sodium by forming ammonia from protein breakdown products The increased excretion of ammonia is therefore to some extent a measure of acidosis

The pigments of urine are nitrogenous The principal one urochrome to which urine normally owes its colour though closely related to urobilin has an independent origin Even when all the bile escapes from the body through a biliary fistula the excretion of urochrome is unaltered Urobilin on the other hand is a reduction product of bile pigment The reduction is effected by bacterial action in the bowel when it is reabsorbed by the blood and excreted by the kidney Normally it is excreted as a colourless chromogen The excretion of urobilin as such may result from increased hæmolysis or from large extravasation of blood and in diseases of the liver and with intestinal putrefaction or obstruction Urobilin gives urine an orange tinge Urobilinogen changes to urobilin on exposure to light and air and this partly accounts for the higher colour of urine on standing The chief interest of uroerythrin of which normal urine contains only a trace is that it gives the urine a reddish orange colour when excreted in appreciable amount as a result of gross liver disease (new growth or cirrhosis) and congestive heart failure It is responsible for the pink colour of urates deposited from concentrated urines in these diseases Traces of two other pigments urorosein and hæmatoporphyrin are present in normal urine

Other nitrogenous constituents of the urine are hippuric acid the purine bases guanine and adenine aminoacids and peptides and traces of basic substances including trimethylguanidine putrescine and cadaverine

Non nitrogenous constituents—These are principally salts Sodium chloride is the most abundant averaging from 10 to 13 g a day It is retained whenever the body retains excess of fluid This explains the reduced output of sodium chloride in such conditions as œdema and serous exudation Reduced salt intake or loss through excessive vomiting are other causes On the other hand the output is much increased in Addison s disease A simple test for chloride is made by adding 10 drops of concentrated nitric acid to 5 ml urine and then add 5 ml 3 per cent silver nitrate solution In normal urine there is an abundant curdy precipitate of silver chloride but if the chlorides are diminished the solution merely appears milky or opalescent Urinary sulphates which are chiefly derived from the sulphur of the protein mole cule are excreted in the urine as inorganic sulphates (about 90 per cent) and the remainder as ethereal sulphates and neutral sulphur Indican (an ethereal sulphate potassium indoxyl sulphate) is present in traces in normal urine it is excreted in excessive quantity in intestinal putrefaction and in simple constipation Less importance is now attached to indicanuria than formerly but it is of interest as an example of a means namely that of conjugation by which the body renders a toxic substance innocuous The phosphates are excreted half as acid phosphates of sodium and potassium and half as earthy phosphates of calcium and magnesium The former are not precipitated on neutralisation while the latter are they come down as amorphous debris which settles as a white deposit If amorphous phosphates separate from the urine before it is passed they make it opalescent or milky (phos phaturia) The amorphous deposit of urates is distinguished from that of earthy phosphates by the fact that it occurs in acid urine is dissolved by heat (about 60 C) and is often stained pink by the adsorption of urochrome and uroerythrin

Crystalline deposits are of varied kind and are briefly as follows Crystals of ammonium magnesium phosphate (triple phosphate crystals) found in urine which has undergone ammoniacal decomposition are described as coffin lids or knife rests Crystals of calcium hydrogen phosphate are uncommon and have the form of simple needles or occur as clusters or rosettes Calcium oxalate crystals are octahedral (envelope crystals) or they may be dumbbell shaped These crystals deposited in

the urine before its passage may cause irritation of the renal pelvis with pain and hæmaturia Uric acid crystals to naked eye examination are distinctive They appear like grains of cayenne pepper at the bottom of a urine glass, and under the microscope assume varied forms like barrels prisms, needles or rods Their colour is due to adsorption of urinary pigments Other crystals to which reference may be made are the thorn apple crystals of sodium or ammonium urate the hexagon crystals of cystine, the sheaves of tyrosine and the rare yellow spherical masses of leucin Urinary deposits often contain starch granules (extraneous origin) These may be either recognised by their form or by the fact that they stain deep blue with iodine

Diastase is the only other substance of importance in the urine Ten to 30 units of diastase (the urinary diastatic index) are normally present but less will be found in some forms of impaired renal capacity and a great deal more in most pancreatic diseases A diastatic index of 50 units suggests a pancreatic lesion, while 100 or more make this certain In severe pancreatitis 300 to 500 may be found

THE ESTIMATION OF RENAL FUNCTION

Renal excretion is the most important mechanism by which the body maintains its remarkably constant chemical composition in varying conditions of nutrition and metabolism Thus renal function includes not only the concentration and elimination of metabolic waste products such as urea but also the regulation of body water and electrolytes by controlled absorption of these substances from glomerular filtrate and in some instances by tubular excretion A full assessment of renal function would involve examination of all these separate mechanisms The development of renal clearance tests has made it possible to investigate separately changes in glomerular filtration and in the tubular reabsorption and excretion of the various urinary constituents In addition abnormal excretion of a substance is often reflected in alteration of its concentration in the plasma Thus renal function may be studied by investigation of glomerular and tubular " handling ' of any blood constituent or by estimation of this substance in the body fluids

The choice and practical value of tests of renal function depends on a variety of circumstances In organic renal disease failure of tubular concentration is usually the earliest indication of impairment of function and may be detected by examination of the specific gravity of the urine or by the urea concentration test Creatinine clearance is the most practicable test for recognising early impairment of glomerular filtration The urea clearance test gives a good indication of progressive impairment of renal function but requires special precautions for accurate results and does not discriminate between organic renal insufficiency and extrarenal (circulatory) nitrogen retention The blood urea level is of obvious value in recognising more advanced failure of glomerular filtration leading to nitrogen retention but again concentration tests are necessary to exclude purely circulatory causes of reduced filtration The specific clearance tests such as inulin clearance for measuring glomerular filtration and Diodrast or *p* amino hippurate clearance for measuring renal blood flow and maximum tubular excretion are of great value in studying variations in renal function in normal subjects but their interpretation in patients with severe renal disease is often doubtful The same applies to clearance measurements of individual normal constituents of the urine Such tests are rarely indicated in the common forms of kidney disease but may be of value in the occasional cases where specific anomalies of tubular function occur in the absence of serious organic renal damage Detailed description of clearance tests is therefore not included here but some practical information on the simpler tests of renal function is given below

Urine Specific Gravity—If the patient is under observation in hospital daily examination of the first specimen of urine passed on waking provides a series of

specific gravity values which gives a useful indication of tubular concentrating power A more accurate test is performed by withholding fluids after breakfast on one day emptying the bladder last thing at night and measuring the specific gravity of the first three specimens passed at hourly intervals after waking next morning If the specific gravity does not exceed 1 020 in any specimen there is definite impairment of tubular function The presence of 1 g per 100 ml albumin in the urine raises the specific gravity 3 points A negative error may be introduced if the specific gravity is measured when the urine is still warm the values then being 3–4 points below readings taken at room temperature

The Urea Concentration Test—Fifteen grammes of urea dissolved in 100 ml water are taken in the fasting state after the bladder has been emptied The urine urea concentration at the end of 1 2 and 3 hours is then estimated (if the blood urea is considerably elevated urea need not be administered) When the urea concentration of the urine exceeds 2 g per 100 ml tubular concentrating power may be taken as unimpaired. Values below this level may however be obtained in normal subjects if absorption of urea is delayed or if the urine volume exceeds 100 ml per hour during the test

Creatinine Clearance—At low blood levels creatinine clearance is a fairly accurate measure of glomerular filtration This test requires only estimation of the creatinine concentration in the blood and in a 3 hour specimen of urine

Phenol Sulphonephthalein (*P S P*) *Excretion*—This dye is partly excreted by the renal tubules and gives a rough indication of tubular dysfunction The percentage excretion of the dye is estimated 2 hours after intramuscular injection or for more accurate information 30 minutes after intravenous injection during this period 60–70 per cent of the injected dye should be excreted in normal subjects The interpretation of results is doubtful if low urine volumes are excreted and occasionally normal figures are obtained when other tests are grossly impaired

In conclusion renal function is influenced by a wide variety of circumstances and changes in glomerular and tubular activity are so diverse that on the one hand no single test can be expected to give an accurate indication of renal impairment and on the other most tests are subject to wide normal variations and errors of interpretation From the practical point of view however the creatinine clearance test gives early evidence of impaired glomerular filtration whilst elevation of the blood urea indicates a more severe degree of glomerular impairment Whether this is due to organic renal damage or extrarenal (circulatory) factors can only be decided by other tests Tubular concentration is usually normal in conditions producing extra renal nitrogen retention an important exception being severe sodium deprivation Thus it is essential in all patients with elevation of the blood urea to look for clinical and biochemical evidence of extrarenal causes The urine specific gravity gives valuable information on tubular concentrating power but after the specific gravity becomes fixed, further deterioration in tubular function can be followed only by quantitative tests such as urine urea concentration At this stage however the blood urea level is probably a more reliable index of progress and is more easily determined

ESTIMATION OF FUNCTION OF KIDNEYS SEPARATELY

This can only be approximately determined but is a necessary preliminary to nephrectomy since it is essential that the opposite kidney shall be functioning normally Some evidence of impaired function may be obtained on intravenous pyelography when it may be seen that concentration is impaired or absent on one side Further evidence may be obtained by observing on cystoscopy the time taken for indigo carmine to appear at the ureteric orifices after intravenous injection of 5 to 10 ml of the dye If more exact information is required urine should be collected from the kidney by ureteric catheterisation The specimen can then be examined for specific gravity albumin pus and bacterial culture

ABNORMALITIES OF THE URINARY SECRETION

1 POLYURIA

Polyuria implies an increased volume in the output of urine, without reference to mere increased frequency of micturition It may be due to

1 Increase in the quantity of fluid imbibed

2 Increase in the molecular concentration of the glomerular filtrate as in diabetes mellitus Less water is thereby reabsorbed by the tubules from the glomerular filtrate

3 Elimination of sodium from the body, i e saline diuresis as after administration of salt or cortisone

4 Incapacity of diseased kidneys to excrete a concentrated urine as in chronic nephritis

5 Diabetes insipidus may arise without any discoverable cause or may be due to disease of the pituitary gland or of the overlying hypothalamus, or to damage in this neighbourhood of syphilitic meningitis of the base of the brain

2 ANURIA

This means suppression of the secretion of urine as opposed to retention and may be due to

1 Acute nephritis or nephrosis, whether the result of an infection or of drugs such as sulphonamides especially sulphathiazole and sulphapyridine turpentine, cantharides and mercuric salts

2 Bilateral obstruction to the ureters

3 Traumatic causes, such as operations on the kidney or trigone of the bladder crushing injuries of the limbs obstetric shock

4 Severe infections such as malaria Weil s disease infected abortion

5 Incompatible blood transfusion

6 Peripheral circulatory failure (shock) Here both low blood pressure and oligæmia reduce glomerular filtration

3 ALBUMINURIA

Albuminuria should be more correctly termed proteinuria—since blood serum contains two proteins—albumin and euglobulin—and either may appear in the urine though search is seldom made for the latter The ordinary tests of heat coagulation nitric acid or salicyl sulphonic acid give positive results with either The presence of euglobulin may be shown by the addition of dilute acetic acid (33 per cent) to urine in the cold The acid is added drop by drop and the precipitation of globulin is shown by an opalescence in the urine to which the acetic acid is added Mucin is also deposited by the addition of acetic acid but it is not redissolved by an excess of acid A more distinctive test is the precipitation of globulin in distilled water Single drops of urine are dropped into a glass vessel containing distilled water As the drop of urine falls through the water it assumes a ring form and the ring has a milky appearance due to precipitated globulin when the latter is present The globulin can be precipitated for quantitative examination by making the urine alkaline with ammonia and then half saturating it with ammonium sulphate

Proteinuria may be classified thus

I WITHOUT ORGANIC DISEASES OF THE KIDNEYS as in—

1 *Functional or orthostatic proteinuria* —This is common in males between puberty and adolescence it is much less common in females of the same age Dukes found it in 16 per cent of all boys entering Rugby School Protein appears in the urine

secreted in the upright posture and is absent from the urine passed on first rising but it may be present in the urine secreted during the first hour of recumbent posture There is no evidence that the amount of protein in the food influences it Severe physical exercise may excite proteinuria in healthy young adults Collier found it present in every one of the Oxford crew of 1906 after rowing a course to such a condition the term physiological proteinuria may fairly be applied When the protein appears apart from exertion the subject is often an anæmic weedy youth with a dull heavy aspect and a tendency to fainting The heart is irritable and the blood pressure unstable and fluctuates with change of posture There may also be a few hyaline casts and frequently calcium oxalate crystals In any case of proteinuria less than 0 1 per cent in amount in a boy or young man the diagnosis of a kidney lesion should not be made unless casts other than hyaline are discovered and unless the blood pressure is definitely and permanently raised If the urine passed on first rising in the morning is albumin free the albuminuria is almost certainly functional

2 *Febrile*—Any acute specific fever may be accompanied by proteinuria due to cloudy swelling of the kidney It should subside soon after the temperature falls to normal This type of albuminuria is referred to again under the heading of Toxæmic Kidney to which it more properly belongs

3 *Congestive*—In heart failure there is usually proteinuria from venous congestion of the kidneys Hyaline casts may also be found Unlike the urine of nephritis the urine is loaded with urates After an epileptic fit there is often a transitory proteinuria probably due to the congested condition of the veins during the fit For a similar reason protein is apt to be present in the urine of any unconscious person

II With Organic Diseases of the Kidneys and Urinary Tract—

1 Nephritis acute and chronic including acute suppurative nephritis focal nephritis periarteritis nodosa and pyelonephritis

2 Acute and chronic ischæmic renal disease including malignant hypertension diabetic glomerulosclerosis severe renal arteriosclerosis and renal infarction

3 Toxæmia of pregnancy and tubular nephroses

4 Amyloid disease of kidney

5 Renal tuberculosis Grawitz tumour and congenital cystic kidneys

6 All conditions of the urinary tract characterised by hæmaturia and pyuria

4 ALBUMOSURIA

Albumose or more correctly proteose may be found in urine during autolysis of the tissues It is not of clinical importance except to distinguish it from Bence Jones proteinuria Bence Jones protein which is found in considerable amounts in the urine of sufferers from multiple myeloma is not a true proteose though possessing similar solubilities It has affinities with native proteins It begins to be precipitated at 40 to 55 C but on approaching boiling point most of the precipitate is redissolved This is probably due to the influence of certain salts in the urine and is not a property of the isolated protein Since organic renal disease may complicate myelomatosis the heat test may be masked by the presence of albumin If present this should be precipitated and the heat test repeated on the filtrate Bence Jones protein also gives a ring of coagulum on contact with strong hydrochloric acid Its recognition is of great diagnostic value as it is pathognomonic of multiple myeloma (see p 1184) Sometimes the Bence Jones protein is spontaneously precipitated causing the urine to appear milky Considerable excess of phosphates may be found in this milky precipitate probably derived from the autolysis of the surrounding bone

True peptone is exceptionally found in the urine in pneumonia and phthisis but is of no clinical importance

5 HÆMATURIA

When blood is intimately mixed with the urine it is held to be in favour of its renal origin Bleeding from the bladder is more apt to occur into the last part of the urine voided while urethral bleeding is said to occur chiefly into the first part. When the quantity of renal bleeding is not great it imparts a smoky appearance to the urine, owing to the conversion of some of the hæmoglobin into methæmoglobin On spectroscopic examination methæmoglobin gives an absorption band in the red in addition to the two bands in the green characteristic of oxyhæmoglobin The chief causes of hæmaturia are best classified as follows

1 *Prerenal*—The altered condition of the blood which occurs for instance in scurvy purpura hæmorrhagica and certain hæmorrhagic fevers leads to the escape of some of the blood through the kidney without any evidence of a definite kidney lesion

2 *Lesions of the kidney* due to (*a*) Nephritis both acute and chronic Hæmaturia is a constant feature of acute nephritis and of exacerbations of chronic nephritis In acute focal nephritis (*e g* complicating subacute bacterial infection) hæmaturia may be the only sign of renal disease

(*b*) Malignant hypertension

(*c*) Local lesions of the kidney *e g* tuberculosis Grawitz tumour congenital cystic kidney, epithelioma of the renal pelvis calculus

(*d*) Renal trauma

(*e*) Infarction of the kidney

(*f*) Drugs such as sulphonamides mercury

3 *Local lesions of the urinary tract*, *e g* ureteric calculus, papilloma and carcinoma of bladder, prostatic enlargement

6 HÆMOGLOBINURIA

This is due to some hæmolytic agent It may be—

1 *Paroxysmal* as in Raynaud s disease and in syphilis Most cases are syphilitic The corpuscles are broken down by a hæmolysin which is present in the blood of 5 to 10 per cent of cases of tertiary syphilis Those who suffer from paroxysmal hæmoglobinuria are presumed to have some constitutional peculiarity which renders them susceptible to this hæmolysin The hæmolysin acts as an amboceptor unites with the red corpuscle in the cold and on return to warmth the normal complement in the plasma causes hæmolysis In addition to this there are some rare forms of non syphilitic paroxysmal hæmoglobinuria

2 *Toxic*—In this group the toxic agent produces the hæmoglobinuria without an additional factor Striking examples of this are blackwater fever (*q v*) in which the hæmoglobin is actually excreted as methæmalbumin poisoning by arseniuretted hydrogen and transfusion of incompatible blood Hæmoglobinuria may also occur in Lederer s anæmia The chemical tests for hæmoglobinuria are the same as for hæmaturia but the microscope will fail to reveal red corpuscles Some of the pigment is excreted as methæmoglobin especially after drugs of the aniline group, nitrites or potassium chlorate

7 PORPHYRINURIA and PORPHYRIA (See p 452)

8 BILIRUBINURIA

Another derivative of hæmoglobin bile pigment appears in all forms of jaundice due to obstruction of the main or intrahepatic ducts In hæmolytic jaundice such as acholuric family jaundice as the name implies bile does not appear in the urine

Bile pigment can often be recognised by noting the tingeing of the froth caused by shaking the urine but is best detected by the green colour given on addition of a solution of iodine to the urine Hunter s diazo reaction is a more delicate test for bilirubin Bile salts are often absent from the urine when bile pigment is present

9 MELANURIA

Melanin only appears in the urine in melanotic sarcoma Garrod has shown that in all other diseases in which melanuria has been recorded the test employed has been unsatisfactory The melanin is excreted as melanogen which darkens on standing and gives a black precipitate on addition of ferric chloride which is soluble in excess of the reagent yielding a black solution A more delicate test is made by the addition of sodium nitro prusside and sufficient caustic soda to render the urine alkaline The ordinary ruby red colour due to creatinine is developed The urine is now made acid with acetic acid and if melanogen is present a prussian blue colour appears

10 ALKAPTONURIA

Alkaptonuric ochronosis is an inborn error of metabolism (Garrod) It is hereditary and scarcely affects health The individual cannot complete the katabolism of the amino acids phenylalanine and tyrosine as a result 2 5 dehydroxyphenylacetic acid or homogentisic acid appears in the urine The urine reduces Benedict s solution on boiling but it does not ferment It darkens on standing or at once on the addition of alkalis It may stain the linen brown When a dilute solution of ferric chloride is allowed to fall drop by drop into urine each drop produces a transitory deep blue colour The urine reduces ammoniacal silver nitrate in the cold giving a silver mirror on the sides of the test tube The black pigment in ochronosis is noticed clinically in cartilaginous tissue An early sign of the disorder is a blue discoloration of the ears especially of the concha and antihelix and later the tragus and antitragus Triangular brown pigmentary deposits with their bases towards the cornea are noted in the scleræ Bluish discoloration of the tendons of hands also occurs In long-standing alkaptonuria a peculiar gobse gait kyphosis and a stooping posture are characteristic features These changes are due to osteoarthritis especially of the vertebral joints

(For other reducing substances in the urine including sugar see p 425)

11 KETONURIA

Ketonuria is a term used loosely to include the appearance in the urine of diacetic acid and its derivatives acetone and β oxybutyric acid Acetone however being merely a decomposition product of diacetic acid is relatively unimportant β oxybutyric acid formerly regarded as the source of diacetic acid is more saturated and less toxic and has been shown by Hurtley to be formed out of diacetic acid by the liver as an attempt at detoxication Diacetic acid is derived from the incomplete oxidation of fats or of the fatty acid groups in protein It is probably always made in small quantities but when there is an abundant consumption of carbohydrate it is completely oxidised In starvation the store of glycogen is quickly exhausted and the body chiefly lives on its fats hence ketonuria Vomiting whether persistent or cyclical will excite ketonuria though without such a degree of intoxication as to cause symptoms Any disturbance of health in infancy and childhood especially a febrile state is liable to cause ketonuria In conditions where the liver is thrown out of gear such as post anæsthetic poisoning ketonuria may occur with toxic symptoms because of the severe disturbance of all metabolic processes But there are other

agents at work besides diacetic acid which may be responsible for those symptoms Only in advanced diabetes do we find toxic symptoms directly due to diacetic acid Here there may be complete inability to utilise carbohydrates so that the body perforce lives on protein and fats If these are freely given in the food the amount of diacetic acid produced may be very large But if a diabetic be starved there is a great drop in ketonuria, showing that most of this is exogenous in origin (see Diabetes) The test used for diacetic acid is the mahogany red colour given on the addition of ferric chloride This has the disadvantage of being masked if the patient is taking salicylates The nitro prusside test was formerly regarded as showing the presence of acetone, but Piper demonstrated that it is really a much more sensitive test than ferric chloride for diacetic acid A crystal of nitro prusside of soda is dissolved in the urine and then a strong solution of ammonia is poured on the top A ring the colour of Condy s fluid speedily develops at the junction of the liquids and spreads upwards The intensity of colour is a rough measure of the degree of ketonuria The reaction is made still more sensitive by previous addition of crystals of ammonium sulphate to saturation (Rothera)

12 DRUGS WHICH ALTER THE COLOUR OF URINE

Methylene blue is used as a colouring matter of sweets and also as an ingredient of certain proprietary pills It used to be given for *Bact coli* infections of the urinary tract gonorrhœa and bilharzia or less commonly as an analgesic in rheumatism sciatica and migraine In small quantities it imparts a green colour to the urine when it may be precipitated with the mucin In larger doses it turns the urine blue It can be recognised by simple filtration because it is adsorbed on the filter papers It can be dissolved from the filter paper by chloroform, and is turned pink by the addition of alkalis Its identity is best proved by loss of colour on adding glucose and alkali Eosin may be used in sweets and turns the urine a fluorescent pink Prontosil and pyridium turn the urine a reddish orange colour though if the urine is alkaline, this may not appear until it is acidified Amidopyrine may have a like effect Rhubarb and senna may turn the urine reddish brown from the chrysophanic acid they contain The urine turns pink on the addition of an alkali Santonin turns the urine a vivid yellow, which becomes rose pink with alkalis Carbolic acid may turn the urine greenish black on standing from the formation of hydroquinone In carbolic acid poisoning the urine withdrawn by a catheter may even be found olive green without exposure to the air Other drugs which may have this effect are salol creosote naphthalene and uva ursi In chronic carboluria ochronosis may occur as in alkaptonuria

Certain drugs can readily be recognised in the urine by some colour reaction Thus salicylates are excreted as salicyluric acid which gives a violet colour on the addition of ferric chloride Copaiba which is precipitated by nitric acid can be distinguished from albumin by the solubility of the precipitate in alcohol On the addition of hydrochloric acid a urine containing copaiba turns cloudy the cloud soon becoming rose pink Iodides in urine give a blue colour with guaiacum and on the addition of hydrochloric acid impart a violet colour to chloroform shaken up with the urine

13 PYURIA

Pus may come from the urethra prostate bladder or kidney The diagnosis of the source is discussed under septic diseases of the kidney The best test for pus in the urine is the microscope If the amount of pus be considerable it will yield a ropy mass on the addition of liquor potassæ If ozonic ether is shaken with the urine bubbles of oxygen are evolved With tincture of guaiacum a blue colour may be given even without the addition of ozonic ether

14 CHYLURIA

True chyluria is due to blocking of the thoracic duct most commonly by *Filaria bancrofti* but sometimes the result of inflammatory or neoplastic conditions with consequent rupture of lymphatics of the bladder through back pressure Fat may be found in the urine in the lipæmia of diabetes, in growths of the kidney and after fracture of long bones when fat may be liberated into the circulation Accidental contamination by an oily lubricant for a catheter and fradulent addition of milk to the urine must be excluded Pseudo chyluria is due to a lecithin compound of globulin and is sometimes found when there is a great excess of globulin in the urine Unlike true fat this substance is not extracted by shaking up with ether

15 PNEUMATURIA

Osler gives the following causes for gas in the urine (1) Mechanical introduction of air in vesical irrigation or cystoscopic examination in the knee elbow position (2) Infection of the urine as by *Clostridium welchii* (3) Vesico enteric fistula An additional cause is infection with yeasts in diabetes

16 CRYSTALLINE DEPOSITS IN URINE

The chief factors in the deposit of *uric acid* crystals as such are high acidity high percentage of uric acid and poverty in mineral salts The first two are the most important especially the first Deposits of urates are usually amorphous These have already been briefly described (see p 1099) *Calcium oxalate* crystals may cause bladder irritability with increased frequency of micturition and occasionally albuminuria and hæmaturia They may arise from ingested oxalates Rhubarb spinach asparagus and sorrel are the foods most likely to produce oxaluria sufficient to excite symptoms for each contain more than 2 g of oxalic acid per kilogram though many other articles of diet contain some oxalates Some individuals seem sensitive to strawberries which however only contain 0 06 g per kilogram

17 AMINO ACIDURIA

Recent light has been thrown on the significance of amino acid excretion by paper chromatography Amino acids may appear in the urine in excess either due to an abnormally high plasma level as in liver disease or due to low renal threshold as in Fanconi s syndrome and familial cystinuria In severe liver disease such as acute yellow atrophy gross amino aciduria occurs and there may be an excess of all the common amino acids in high concentration In chronic liver disease an excess of cystine is commonly found In hereditary (familial) cystinuria cystine is continuously excreted in large quantities crystals may appear in the urine and cystine calculi tend to form in these cases lysine and arginine are also excreted in increased amount In Fanconi s syndrome the cystinuria is part of a generalised disturbance of urinary amino acid excretion and abnormal amounts of other amino acids appear in the urine Resistant rickets and deposition of cystine in the tissues (cystinosis) occur in the Fanconi syndrome but stone formation does not occur

CIRCULATORY DISTURBANCES

1 *Passive congestion* —Anything which raises the pressure in the renal vein must produce a passive congestion of the kidney Failing compensation in heart disease

and hypertension is the commonest cause, but it may also be brought about by respiratory diseases or by pressure on the renal vein by abdominal tumours or ascities A transient congestion may result from an epileptic fit

The cardiac kidney as it is called, is the most typical example of passive congestion The organ is firm and dark in colour, especially the pyramids The capsule strips normally The stellate veins are engorged The kidney may drip with blood on section and if placed in a dish after section soon exudes œdematous fluid

The urine is scanty, high coloured and of high specific gravity Unlike the urine of chronic nephritis it is loaded with urates It contains a variable amount of albumin and hyaline casts with a few red blood corpuscles if the congestion is at all considerable A moderate degree of nitrogen retention may result (up to 100 mg per cent blood urea) but tubular concentrating power is unaffected The prognosis and treatment are those of the cardiac condition causing it Stimulating diuretics are of much more service than in nephritis since there is no primary disease of the secreting structures Organic mercurial preparations are especially effective

2 *Infarction* —This may be due to embolism, *e g* in rheumatic carditis or infective endocarditis or to thrombosis in an atheromatous renal artery Obstruction of large arteries leads to anæmic infarcts, 'map like areas of coagulation necrosis roughly wedge shaped but with irregular edges and with the base reaching the surface of the organ Their formation may cause a sudden pain in the loins if they are large Either of these conditions will cause both albuminuria and hæmaturia.

3 *Thrombosis of the renal vein* —This is rare and is usually significant of a terminal infection as in a marasmic infant In thrombosis of the inferior vena cava the process may reach as high as and spread into the renal vein This would produce the same effects as the cardiac kidney but in a much more intense form Bilateral renal vein thrombosis may arise from no apparent cause and may produce a picture indistinguishable from that of nephrosis

URÆMIA

Uræmia literally means retention of urine in the blood so that by derivation the principle features should be due to failure of excretion of waste products of metabolism The functional disturbance in renal failure is however much more complex than this Excretion of waste products by the kidney is only a small part of its total function, and renal failure can only be fully understood when the kidney is considered as the chief executive organ of the homeostatic mechanism of the body That is acting under the influence of the adrenal and pituitary glands and other controlling factors not yet elucidated the kidney plays a vital part in maintaining the various body equilibria These include total water content of the body sodium and potassium regulation, acid base balance and in all probability maintenance of normal blood pressure It is obvious therefore that renal failure will produce complex and varied symptoms related to these functions The picture is further complicated by the fact that renal efficiency is itself considerably affected by disturbance of these body equilibria Thus salt deficiency alkalosis and hypotension all have a serious effect on the process of urine formation At the outset therefore it is necessary to distinguish between *extrarenal uræmia* due to these factors and *primary renal failure* due to organic disease of the kidneys and further to appreciate that the latter may be complicated by the former

NORMAL KIDNEY FUNCTION —(1) *Excretion of waste products* —These are almost entirely the end products of protein metabolism urea uric acid creatinine and ammonia In addition organic acids may be excreted either alone or after being conjugated with other substances by the liver

(2) *Acid base balance* —The cations excreted by the kidney are sodium potassium

ammonium calcium and magnesium The anions are chloride phosphate sulphate and organic acid radicals The kidney compensates for changes in the acid base balance of the blood largely by conservation of base This it performs *e g* in severe acidosis by increase in the reabsorption of sodium in the excretion of hydrogen ions and in the elaboration and excretion of ammonia by the renal tubule cells

(3) *Body water* —Excessive water drinking leads to water diuresis whilst excessive loss of fluid due to vomiting, sweating or diarrhœa leads to oliguria This com pensatory process is due to the action of the posterior pituitary anti diuretic hormone which decreases or increases reabsorption of water by the renal tubules Disorder of this mechanism is illustrated by the gross polyuria of diabetes insipidus

(4) *Electrolyte control* —Conservation of body sodium is a priority function of the kidney and the absorption of sodium by the tubules is under the direct control of the salt hormone of the adrenal cortex Breakdown of this control occurs in Addison s disease and leads to excessive sodium loss in the urine with consequent reduction in the volume of extracellular fluid The mechanism by which the renal tubules regulate potassium excretion is not fully understood Phosphate reabsorption is controlled by the parathyroid glands excessive elimination in hyperparathyroidism leads to the gross disturbance of calcium metabolism which characterises this disorder Other rare functional tubular anomalies of electrolyte control occur in nephrocalcinosis and the Fanconi syndrome

(5) *Maintenance of the arteriolar resistance* which determines diastolic blood pressure is in some way related to kidney function, since diastolic hypertension is a common feature of renal disease and experimental interference with renal blood flow in animals regularly produces high blood pressure That this is not due to renal failure in the ordinary sense of the term is shown by the fact that unilateral renal artery constriction can lead to sustained hypertension There is a possibility that the adrenal cortex is also concerned in this function of the kidney since such experi mental hypertension is abolished by adrenalectomy

Mechanism of Urine Formation —There are roughly one million nephrons in each kidney and the renal blood flow through the glomeruli is about 1 3 litres per minute *i e* one third of the cardiac output Urine is formed by a combination of glomerular filtration with selective tubular absorption Glomerular filtration is purely physical and is brought about by an effective filtration pressure which is the resultant of the blood pressure and osmotic pressure in the glomerular capillaries The glomeruli filter about 170 litres per day and the filtrate contains all the constituents of blood plasma except that protein is present in only minute amounts the specific gravity of glomerular filtrate is approximately 1 010 Clearance of substances from the blood is almost entirely a function of glomerular filtration Selective *tubular reabsorption* is responsible for changing the glomerular filtrate into urine It therefore involves the reabsorption of all the water in the glomerular filtrate except some 1 500 ml together with the greater part of the useful substances such as sugar and chloride By this massive reabsorption of water the tubules concentrate waste products particu larly urea about one hundred times Since the urine is normally hypertonic (S G 1 020 to 1 030) compared with glomerular filtrate it is obvious that the fluid absorbed by the tubules must be hypotonic *i e* in health the renal tubules do osmotic work in concentrating the urine Even when tubular function is impaired and no osmotic work is done (*i e* when the urine specific gravity is fixed at 1 010) there is still a selective reabsorption of useful substances which permits considerable concentration of urea

Primary Renal Failure —Primary renal failure is due to destruction of nephrons by organic kidney disease At the outset two main types must be recognised The more common is chronic uræmia due to progressive Bright s disease or other destruc tive lesions Less common is acute uræmia to which reference is made under the heading of Traumatic Anuria

(A) CHRONIC URÆMIA

In this form of uræmia impairment of tubular function precedes and exceeds impairment of glomerular filtration, since the epithelial cells of the tubules are more susceptible to noxious agents than is the vascular structure of the glomerulus Furthermore the kidney has a very considerable physiological reserve so that considerable organic damage may occur before the usual tests of tubular or glomerular function can be shown to be impaired We must therefore recognise three stages of renal failure

(1) *Reduction of renal reserve* —In this stage the blood urea and urinary concentrating power are both normal but tests devised to measure the total excretory mass such as diodone clearance may indicate a reduction below the normal This is found for example in severe benign essential hypertension and in renal arteriosclerosis The practical point here is that if a severe strain is imposed on the kidneys for example by a surgical operation or the onset of heart failure or hæmorrhagic shock, it may lead to a severe and sometimes fatal uræmia

(2) *The stage of impaired tubular concentrating power* —The earliest clinical symptoms of renal inefficiency appear at this stage and consist of nocturnal frequency with later polyuria and thirst The limits of specific gravity of the urine are narrowed and there is eventual fixation around 1 010 The urine urea concentration falls below 2 g per cent and this test is a useful measure of subsequent deterioration after the urine specific gravity is fixed This intermediate stage of renal impairment may persist for many years before the blood urea starts to rise Nevertheless polyuria has in most cases of chronic renal disease a limited duration owing to the progressive destruction of glomeruli Persistent polyuria is usually observed only in forms of nephritis in which the tubules are primarily or predominantly involved *e g* ascending pyelonephritis with congenital dilatation of the urinary tract

(3) *Failure of glomerular function* —In this final stage the glomerular filtrate volume falls below the limiting value at which the blood can be cleared of urea The symptoms of uræmia which follow are not however, solely attributable to elevation of blood urea, but are referable to a complex disturbance of function which has already been discussed

THE CLINICAL SYNDROME OF CHRONIC URÆMIA —The clinical syndrome of chronic uræmia results from a combination of excretory failure disturbance of body equilibria and hypertensive manifestations In general those symptoms which are due to excretory failure appear late and may be seen only in the terminal stages whilst hypertensive symptoms are often amongst the earliest manifestations of the disease Elevation of blood urea in itself is not responsible for the variety of symptoms since patients with gross nitrogen retention but without hypertension may be free from symptoms The real cause of the varied manifestations which are often attributed to the retention of waste products is quite obscure Most prominent amongst these are digestive symptoms—anorexia nausea vomiting and hiccough, diarrhœa is infrequent Anæmia is a common complication and is refractory in type Acidosis due to failure of ammonia formation by the kidney leads to the classical usually terminal harsh deep regular acidotic breathing first described by Kussmaul in diabetic acidosis Severe dehydration and sodium deficiency may be due to polyuria and vomiting and these in turn may greatly aggravate the renal failure Increased muscular irritability leading to cramps and twitchings and occasionally to tetany, are due to a complex disturbance in the ionic balance which regulates nervous and muscular excitability, no uniform abnormality of blood calcium is found Irritation of the skin is common and so called urea frost may sometimes be observed on the face There is an increased tendency to hæmorrhage which may cause purpura bleeding into joints or gastro intestinal hæmorrhage A sterile pericarditis is a not uncommon terminal complication Ultimately excretory failure results in drowsiness

disorientation and fatal coma In the very chronic uræmia which occurs in patients with little or no hypertension disturbance of calcium and phosphate excretion leads to decalcification of bone and deposition of calcium in other tissues such as the arterial walls muscles and kidneys Decalcification of the bones in young children may lead to a picture indistinguishable from vitamin D deficiency rickets while in older subjects there may be multiple cystic degeneration of bone such as occurs as a result of hyperparathyroidism marked hyperplasia of the parathyroid glands occurs in chronic uræmia

The hypertensive manifestations of chronic uræmia are referable to the heart the brain and the retina Heart failure is common in hypertensive Bright s disease and predominantly affects the left ventricle with consequent pulmonary congestion and œdema Renal asthma is the same as cardiac asthma and consists of attacks of paroxysmal usually nocturnal dyspnœa due to pulmonary œdema The development of heart failure further aggravates the renal dysfunction Organic cerebral vascular lesions occur as in any other form of hypertension If the malignant phase develops there may be attacks of encephalopathy consisting of disorientation headaches convulsions transient blindness and coma Exudates and hæmorrhages appear in the retina and when these affect the macula impairment of vision results The development of papillœdema is diagnostic of the malignant hypertensive phase Added to this picture of excretory failure and hypertension are the effects of general malnutrition and hypoproteinæmia due to anorexia vomiting and albuminuria It is not surprising therefore that in the terminal stages many patients with uræmia develop generalised œdema the mechanism of which may be partly cardiac partly renal and partly nutritional

(B) ACUTE URÆMIA

Acute uræmia is described under Traumatic Anuria (p 1128) It is characterised by a total failure of the nephron leading to suppression of urine This form of uræmia is also seen in acute nephritis when anuria occurs in the early stage

Extra Renal Nitrogen Retention —This term is preferable to extra renal uræmia since the disturbance is usually limited to a moderate elevation of blood urea (rarely over 100 mg per cent) unassociated with the various complex disorders described above The immediate cause of extrarenal nitrogen retention is some impairment of the renal circulation leading to diminished renal blood flow or lowered filtration pressure or both Such disturbances arise in oligæmic states such as result from hæmorrhage or from severe dehydration The latter may be due to repeated vomiting diarrhœa massive œdema formation or salt deficiency as in Addison s disease A similar degree of nitrogen retention is produced by severe heart failure Glomerular filtration pressure is lowered by shock or by other causes of low blood pressure such as Addison s disease In all these circulatory disturbances the effect is primarily on glomerular filtration so that the blood urea is often found to be elevated whilst tubular concentrating power is normal the urine is highly coloured and the urine output greatly diminished If the circulatory disturbance is severe and very prolonged tubular function is affected and concentrating power is diminished Epithelial cell damage may occur and a tubular nephrosis results which may resolve but leave behind calcification of the epithelium It is important to realise that primary renal failure may be aggravated by extrarenal factors and that correction of the latter may greatly improve renal function

Treatment of Uræmia —This is fully discussed under the treatment of chronic Type 1 and Type 2 nephritis (chronic uræmia) and of traumatic anuria (acute uræmia)

RENAL HYPERTENSION

The occurrence of high blood pressure in some cases of kidney disease was known to Bright The subject has in recent years gained steadily in importance as

experimental evidence has revealed the close relationship between hypertension and development of organic renal damage Goldblatt's experiment in which sustained hypertension was produced in dogs by renal artery occlusion first suggested a mechanism by which renal disease might elevate the blood pressure It has subsequently been shown that many types of experimental renal damage in different species of animals will give rise to hypertension Although it seems probable that some form of circulatory restriction is common to all, the exact nature of the hæmodynamic disturbance which leads to elevation of blood pressure is not yet understood Some important relationships have, however been established The work of Wilson and Byrom showed that sustained hypertension could be produced in rats by incomplete occlusion of one renal artery without interfering with the opposite kidney so that renal insufficiency in the usually accepted sense of the term is not necessary for the development of hypertension Furthermore, organic renal damage is not a necessary pre requisite since high levels of blood pressure were produced although the ischæmic kidney remained histologically normal It was also demonstrated in these experiments that arteriolar necroses with associated glomerular and tubular lesions found in malignant hypertension were produced in the opposite kidney but were absent from the clamped kidney From this it was deduced that the renal lesions which characterise malignant hypertension are in fact the result and not the cause of the high blood pressure in this disorder The common occurrence of similar hypertensive lesions in primary renal disease was also thereby explained Wilson and Byrom went on to postulate that since hypertension can produce occlusive renal vascular lesions a vicious circle may be established which leads to progressive renal damage and further hypertension Such a vicious circle would account for the rapidly progressive course of malignant hypertension, whether renal or essential in origin, and the dramatic manner in which progressive deterioration may be checked when the blood pressure is lowered for example by removal of a single diseased kidney indicates the possibility and importance of breaking the sequence More recent experiments have shown that renal hypertension persists after total nephrectomy so that an extra renal mechanism is in some way involved It seems probable that the adrenal cortex plays a role in this mechanism since adrenalectomy abolishes experimental renal hypertension Moreover administration of salt hormone or increase in sodium chloride intake can act as an effective substitute for the adrenal cortex in maintaining the hypertension A tentative hypothesis is put forward therefore that normally the kidneys inhibit or inactivate an extrarenal pressor mechanism which depends on electrolyte distribution in the arterioles Damage to the kidneys or their removal interferes with this renal inactivation and leads to a rise in blood pressure Much further evidence is required before this hypothesis can be regarded as established but there are many clinical observations such as the well known effect on the blood pressure of sodium restriction on the one hand or increased salt intake on the other which have an obvious relevance to this hypothesis

The varieties of high blood pressure encountered in different forms of renal disease cannot yet be fully related to the underlying lesion Chronic renal disease progressing to renal failure without hypertension is rare but may be encountered in chronic Type 2 nephritis (chronic nephrosis) amyloid disease chronic pyelonephritis and congenital lesions particularly those associated with dilatation of the urinary tract Renal hypertension becomes malignant *i e* papillœdema develops in about a third to one half of all cases *i e* much more commonly than is observed in *essential hypertension* Development of the malignant phase is usually followed by rapid deterioration of renal function and death in 6 to 12 months Nevertheless a temporary remission with subsidence of papillœdema may occasionally occur spontaneously or after reduction in the blood pressure level by sympathectomy hexamethonium drugs or salt restriction

Hypertension due to Unilateral Renal Disease.—Many cases have been

reported in which unilateral renal disease has led to the development of severe hypertension and this may be of the malignant type Secondary hypertensive changes may occur in the contralateral kidney and the histological picture of malignant nephrosclerosis is sometimes found post mortem in such kidneys It is therefore important especially in young subjects presenting with hypertension but without impairment of renal function to search for a possible unilateral lesion Intravenous pyelography may reveal a nonfunctioning kidney or unilateral hydronephrosis or gross contraction on one side with a hypertrophied kidney on the other In such cases nephrectomy may bring about prompt reversal of papillœdema and restoration of blood pressure to the normal level even after many years of severe hypertension A great variety of lesions may be found in the diseased kidney, the most common being chronic pyelonephritis in a congenitally abnormal kidney Other causes of unilateral renal disease which may lead to hypertension are atheromatous obstruction of a main renal artery tuberculosis hydronephrosis renal cysts and tumours

RENAL ŒDEMA

Anasarca was the main clinical feature described by Bright in patients with organic kidney disease Nevertheless our knowledge of the mechanism of renal œdema is no more exact than our understanding of hypertension While in the majority of patients more than one factor is involved it must be recognised that there is a form of fluid retention directly attributable to kidney disease and it is this factor which is still obscure

Pathology of Oedema —Oedema of all forms is the result of water and sodium retention in the tissues In health the extracellular fluid volume is maintained constant by a balance of physical and chemical forces The physical component is the resultant of the hydrostatic pressure of the blood and plasma protein osmotic pressure and these forces control the tissue circulation *i e* the circulation of fluid from the arterial end of the capillary into the tissues and back from the tissues into the venules Increase of hydrostatic pressure as in right heart failure or lowering of osmotic pressure due to hypoproteinæmia will favour accumulation of fluid in the tissues The chemical factors are those responsible for the maintenance of a constant extracellular fluid volume and the most important of these is the salt hormone of the adrenal cortex which directly influences reabsorption of sodium by the renal tubules Administration of the hormone in excessive doses will produce œdema as will failure of tubular function in anuria unless salt and water intake are restricted This hormonal control thus maintains a balance between intake of sodium and water tissue fluid content and excretion by the kidneys

Renal Oedema —*Characteristics* —Anasarca occurs only when both kidneys are diseased In the absence of complicating factors *e g* in acute nephritis œdema is sudden in onset and has a generalised distribution affecting the face trunk and legs It tends to be most marked in the early morning and diminishes with activity in contrast to cardiac œdema In severe cases serous effusions and pulmonary œdema may be produced Clinically the œdema can be recognised by pitting on pressure although there may be in adults retention of half a stone of excess fluid before pitting œdema is demonstrable

Causation —In many patients with Bright s disease several secondary factors play a part in the development or maintenance of œdema These are hypoproteinæmia heart failure and anæmia

Hypoproteinæmia —In the nephrotic syndrome the plasma proteins fall to a low level as a result of heavy albuminuria More albumin than globulin escapes in the urine owing to the smaller size of its molecule thus the lowering of the protein osmotic pressure of the blood is chiefly due to a fall in its albumin content It is usual to find œdema when the total proteins fall below 5 g per cent or the albumin

below 2 g per cent It is probable that hypoproteinæmia contributes to the generalised œdema of many patients with Bright s disease not only those with the nephrotic syndrome but also in the early and late stages of Type 1 nephritis when protein loss may lead to considerable lowering of plasma proteins Nevertheless even in Type 2 nephritis hypoproteinæmia is not the primary cause of œdema since in the early stages generalised œdema may be present with a normal plasma protein level and in any patient massive diuresis with disappearance of œdema may occur without any significant elevation of the blood protein level

Increased Venous Pressure —This factor may contribute to œdema in chronic hypertensive Bright s disease with manifest heart failure and in the occasional cases of acute Type 1 nephritis where heart failure is a complication It cannot however be held accountable for the generalised œdema which occurs in the majority of patients with nephritis Anæmia may contribute to œdema especially in the uræmic stage of chronic nephritis when hæmoglobin levels may fall very low The effect is probably attributable to aggravation of myocardial failure

Sodium Retention —Sodium and water retention are manifestly present in renal as in other forms of œdema restriction of salt in the diet may produce some improvement while increase in sodium intake may increase it We have at present no reason to incriminate either the adrenal cortical hormone or renal retention of sodium due to diminished glomerular filtration or increased reabsorption by the renal tubules In fact glomerular filtration tends to be high in nephrotic œdema and there is no evidence in any form of Bright s disease of inability to excrete sodium unless there is suppression of urine When renal insufficiency develops the tendency is towards excessive sodium loss due to acidosis and failure of ammonia formation by the kidney in occasional cases this may progress to gross salt deficiency There is no justification for the idea that increase in capillary permeability is a factor in salt retention since the capillaries are completely permeable to electrolytes in health and disease Increase in permeability to protein in acute nephritis has not been satisfactorily demonstrated but it is unlikely that this could play a rôle in œdema formation since the proteins themselves are in a state of dynamic equilibrium between blood and tissues

Treatment —The treatment of renal œdema is described under Acute and Chronic *Glomerulo nephritis*

BRIGHT'S DISEASE

Bright s ' Disease ' is in fact a syndrome consisting of albuminuria œdema and (usually) high blood pressure associated with organic kidney disease The majority of patients presenting with this clinical picture are suffering from glomerulo nephritis in its acute or chronic forms Other diseases which may produce the syndrome are *amyloid nephrosis chronic pyelonephritis, malignant hypertension and diabetic* glomerulosclerosis

Classification of Bright s Disease

A Nephritis
- I Glomerulo nephritis
  - Type 1 (synonym acute hæmorrhagic nephritis)
  - Type 2 (synonym parenchymatous nephritis including lipoid nephrosis)
- II Pyelonephritis

B Renal Vascular Disease
- The kidney in essential hypertension—(1) benign (2) malignant
- Senile arteriosclerosis
- Diabetic glomerulosclerosis

C Miscellaneous Conditions
- Amyloid nephrosis
- Traumatic anuria
- Toxæmia of pregnancy
- Toxic nephrosis

GLOMERULO NEPHRITIS

In describing glomerulo nephritis most of the confusion in the past has arisen because names have been given to cross sections of the disease at different stages Hence glomerulo nephritis running a continuous course in the same patient might at different times be labelled acute hæmorrhagic nephritis subacute parenchymatous nephritis chronic interstitial nephritis azotæmic nephritis This cross sectional terminology can only be avoided by a long term study of nephritis from both its clinical and pathological aspects When this approach is followed we arrive at a classification of the *courses* of nephritis such as was introduced by Volhard and Fahr in 1914 In addition recent information derived from experimental pathology and physiology of the kidney has made it possible to relate various disorders of function such as hypertension œdema and uræmia to different organic lesions of the kidney A long term clinical and pathological study of some 600 cases of Bright s disease by Ellis and his colleagues at the London Hospital showed that the many clinical syn dromes of glomerulo nephritis were related to two main types of pathological process which were termed Type 1 and Type 2 nephritis Type 1 is usually preceded by a streptococcal infection Its onset is acute with hæmaturia as a prominent feature The prognosis is good 80 to 90 per cent of patients recovering completely In the remainder according to the severity of the glomerulo nephritis death may occur in the acute stage or after a rapidly progressive course running a period of months or a slowly progressive course lasting from years to decades Type 2 nephritis has an insidious onset with œdema which tends to increase and persist for months or even years Hæmaturia is not a prominent feature but albuminuria is severe and is associated with gross depletion of plasma proteins Recovery is rare and is practically limited to cases without hypertension The great majority of patients continue with albuminuria and recurrent œdema for many years before renal failure develops The morbid anatomical changes correspond closely with these clinical courses In Type 1 nephritis the lesion is diffuse and severe at the onset but in most cases resolves completely In Type 2 nephritis there is a less intense diffuse glomerulo nephritis which gradually progresses in severity and at all stages presents a characteristic involvement of the glomerular capillaries

TYPE I NEPHRITIS

Synonyms —Acute Hæmorrhagic Nephritis Acute Diffuse Nephritis

Most cases of nephritis presenting with acute onset are of this type The disease is commonest in children and adolescents but may occur at any age

Ætiology —Scarlet fever and streptococcal tonsillitis are the common preceding infections Sometimes the patient complains of a cold or a chill without sore throat Less frequent preceding infections are otitis media pneumonia peritonitis erysipelas impetigo boils and pyogenic dermatitis Severe burns may be followed by nephritis possibly due to secondary infection In time of war nephritis may occur in epidemic form for example the trench nephritis of the War of 1914–1918 In these outbreaks the nature of the primary infection may be obscure

Pathology —Microscopically the characteristic feature in the acute stage is increase in cellularity of the glomerular tufts due to proliferation of endothelial cells and infiltration with polymorphonuclear leucocytes Hæmorrhage into Bowman s capsule

is common, and collection of red cells and leucocytes may be seen in the tubules In severe cases fibrinoid necrosis of the glomerular arterioles and even of the glomerular capillaries occurs In the rapidly progressive course the main feature is epithelial crescent formation (proliferative capsulitis) Vascular necroses are common and the tubules may show hyaline droplet degeneration, the interstitial tissue is infiltrated with acute inflammatory cells In the slowly progressive course damaged glomeruli become organised and disappear, interstitial fibrosis is extensive and in the later stages acute and chronic lesions of the glomeruli and vessels are found—focal necroses capsular adhesions necrotising arteriolitis—which are the result of severe hypertensive damage This ultimately leads to focal scarring of the kidney with marked tubular atrophy dilatation of the intervening tubules and hyaline cast formation The final stage is sometimes termed secondary contracted kidney or chronic interstitial nephritis

Symptoms —The onset is usually acute though occasionally it may be insidious In the latter instance the patient may complain of biliousness nausea vomiting and abdominal pain with headache and sometimes diarrhœa before the onset of renal symptoms In the cases with acute onset there may be more or less severe pain in the back and œdema soon develops It usually starts in the face, the legs and scrotum are generally involved next and the swelling soon spreads all over the body Occasionally the dropsy is curiously localised and fugitive Though dyspnœa is not regarded as a common feature of acute nephritis most patients admit to it on direct questioning and if cardiac failure occurs it may be a prominent symptom There is usually only slight fever though occasionally a temperature of 102° or 103 F may be reached, this may be due to persistence of the original infection The pulse rate is increased and the blood pressure is generally raised The skin may be dry and itching with occasionally a papular or erythematous eruption Retinal hæmorrhages may occur but very rarely

The urine is greatly reduced in volume and may be entirely suppressed 8 to 12 oz would be an ordinary figure It is dark in colour and usually contains obvious blood This may render the urine as dark as porter but it may be bright red or merely smoky Sometimes the blood forms a flocculent reddish brown precipitate The urine is usually loaded with albumin and casts will be found on microscopical examination At first blood casts and epithelial casts will alone be found but at a later stage granular and hyaline casts appear Leucocytes are present often in large numbers Isolated renal cells transitional epithelium and squamous cells from the lower urinary tract are also commonly found The urine is sterile on culture A sudden increase in urine output after a few days is a sign of definite improvement due to elimination of œdema fluid

Slight impairment of renal function is common the blood urea being moderately raised Some degree of impaired concentrating power is found in the more severe cases

Complications —(1) *Acute heart failure* —Shortness of breath may be a presenting feature and in severe cases acute pulmonary œdema may occur This complication is found in patients who have a marked rise in blood pressure and demands urgent treatment

(2) *Hypertensive encephalopathy* —The symptoms are sudden in onset and include convulsions blindness mental excitement severe headache, vomiting and transient palsies Coma sometimes develops Severe hypertension is present but the renal function in these patients is good With adequate treatment recovery is the rule

(3) *Infections* —Not infrequently a flare up of the primary infection or the incidence of a new infection may produce a recrudescence of the nephritis Modern therapy has lessened the risk of these infections which were previously often fatal

(4) *Oliguria* —Diminution in the urine output may be due to (1) actual suppres

sion in severe cases or (2) extrarenal factors such as vomiting gross œdema acute heart failure or therapeutic fluid restriction Marked oliguria occurs when there is severe kidney damage and most frequently when there is no hypertension

Diagnosis—The combination of dropsy hypertension albuminuria hæmaturia casts and scanty urine usually makes the diagnosis quite easy The differential diagnosis of acute nephritis from an exacerbation of chronic nephritis may be difficult Definite evidence of cardiac hypertrophy and arterial changes are in favour of the latter An infarct in the kidney which causes a pain in the back and hæmaturia may simulate nephritis but there is no œdema nor are casts present in the early stages Great reduction in the volume of urine is not usual Signs of septic endocarditis would suggest infarction In malignant nephrosclerosis there may be a smart hæmorrhage but the presence of papillœdema and the cardiovascular signs would lead to a correct diagnosis The renal hæmorrhage in the early stage of new growth of the kidney is so profuse that confusion with acute nephritis is not likely to occur Moreover epithelial casts would not be found though a large blood cast from the pelvis of the kidney is a very characteristic feature Pyelitis may give rise to some confusion as there may be small hæmorrhages especially at the beginning The presence of micro organisms in a catheter specimen and abundant pus cells in the absence of casts will generally make the diagnosis clear Moreover general dropsy does not occur in pyelitis unless it sets up severe nephritis as a sequel In any cases of hæmaturia especially when it is associated with profound constitutional disturbance loss of weight, tachycardia, continued fever and peripheral neuritis the diagnosis of periarteritis nodosa must be considered (*q v*)

Prognosis and Progressive Courses—The prognosis in Type 1 nephritis is good and 80 to 90 per cent of patients recover completely Second attacks after complete clinical recovery are extremely rare In the early stage suppression of urine is the most serious prognostic symptom and death in the acute stage is most commonly due to persistent anuria If this lasts more than a week the outlook is very grave but recovery has been known to occur after 14 days anuria In such severe cases hypertension may be absent and persistent vomiting may lead to extra renal uræmia the blood urea rising as high as 300 mg per cent Severe hypertension (around 200 mm mercury systolic) may also be a bad prognostic sign in the acute stage in terms of immediate complications *i e* left ventricular failure and hypertensive encephalopathy Heart failure as a complication has a much more serious significance than encephalopathy Persistent hæmaturia is usually evidence of a progressive lesion but recovery has occurred in cases where visible blood persisted in the urine for three months Microscopic hæmaturia has a less serious significance particularly in younger subjects since it may be orthostatic in origin and complete recovery may occur after red cells have persisted in the urine for a year or more The same is true of a persistent trace of albumin in the urine Recrudescences usually marked by return of hæmaturia during the first few weeks often following recurrence of the initial infection may greatly prolong convalescence or lead to chronic nephritis Recovery tends to be slower in the elderly than in young subjects About 5 per cent. of patients with acute nephritis die in the acute stage *i e* the first 2 or 3 weeks the causes being anuria pulmonary œdema due to heart failure or infection

(1) *Rapidly progressive course*—This occurs in about 5 per cent. of patients and is due to a severe irreversible glomerulo nephritis characterised by epithelial crescent formation Clinically there is persistent hæmaturia hypertension and œdema which is often severe and generalised Progressive renal failure occurs over a period of 6 months to 2 years and there may be a malignant hypertensive termination with papillœdema encephalopathy and left ventricular failure

(2) *Slowly progressive course*—In a series of cases of acute nephritis studied by Ellis only about 5 per cent followed this course Nevertheless in any clinic there

will be a large proportion of patients with chronic Type 1 nephritis since the disease may last for decades Moreover about half these patients will give no history of acute nephritis, but first present with symptomless albuminuria or hypertension often discovered on routine examination or with hypertensive symptoms or uræmic manifestations later in the disease The natural history and prognosis is decided by two factors the severity of the residual nephritic lesions and the incidence of hypertension. Where the nephritic damage is severe there is no hard and fast demarcation from cases running a rapidly progressive course There is severe destruction of the kidney and uræmia may develop insidiously in 5 to 10 years with or without marked hypertension Polyuria may appear when tubular concentrating power becomes impaired, but as destruction of nephrons progresses urine output returns to normal and in the final stages there is usually oliguria Anæmia is often found long before the onset of uræmia and is probably due to malnutrition In chronic renal failure refractory anæmia develops and this is in some patients the presenting feature of the disease. Further symptoms are described under uræmia (p 1010) With less severe degrees of residual renal damage the patient may continue for 30 years or more and during this stage may be free from symptoms but regular examination of the urine shows persistent albuminuria During this long stage inflammatory elements are usually absent from the urine and acute recrudescences of nephritis are rare At any time however and more commonly in males the blood pressure may be observed to rise, often over a period of months and rapid deterioration in renal function may then occur About 50 per cent of patients develop the malignant hypertension syndrome This complication may be the first manifestation of renal disease and it may be very difficult if there is no past history of acute nephritis to decide whether the hypertension is nephritic or essential In general patients with malignant essential hypertension are found to have only slight impairment of renal function when papillœdema is first discovered whereas in chronic nephritis renal failure is usually advanced at this stage Although the ultimate prognosis is poor in both conditions the results of treatment by sympathectomy or hexamethonium compounds are somewhat better in malignant essential than in malignant renal hypertension The clinical features of the malignant termination in chronic Type 1 nephritis are identical with those of malignant essential hypertension (p 914) except that symptoms of renal failure are more pronounced Attacks of hypertensive encephalopathy producing headaches blindness convulsions disorientation and coma may occur as in acute nephritis this condition is reversible and improves after the blood pressure is lowered by hexamethonium drugs In chronic nephritis however, the improvement is usually short lived because of the associated irreversible uræmia

OTHER FORMS OF ACUTE NEPHRITIS —*Acute focal nephritis* is characterised clinically by an attack of hæmaturia occurring in the course of an acute infection such as otitis media Hypertension œdema and renal failure are absent and recovery usually takes place after a few days Occasionally however attacks of focal nephritis recur at long intervals and in such patients albuminuria may persist indicating residual renal damage If the attacks continue hypertension and renal impairment eventually appear and the histological picture in this late stage is indistinguishable from that of chronic Type 1 nephritis

In subacute bacterial endocarditis nephritis when it occurs is characteristically focal but may be diffuse Histologically the focal lesion consists of glomerulitis with hæmorrhage into Bowman s capsule which leads to epithelial crescent formation and later to characteristic boat shaped collagen crescents Although this lesion was at one time thought to be embolic it is doubtful whether there is any ætiological difference between the focal and diffuse forms of glomerulo nephritis in bacterial endocarditis A similar state of affairs occurs in *Henoch Schonlein purpura* where renal involvement may take the form of hæmaturia alone or the full picture of nephritis may develop with hypertension œdema and renal failure In the latter case the prog

nosis is usually poor This form of nephritis is probably allied to that occurring in *periarteritis nodosa* which may present with a typical attack of acute nephritis and purpura In both conditions acute necrotising arteriolitis may be found in the kidney and in other organs Acute nephritis is occasionally seen in patients with acute rheumatic carditis but so rarely that the association may be fortuitous

Treatment —ACUTE STAGE —In the acute stage the patient should be put to bed and kept completely at rest as in a case of acute carditis Daily observations of the blood pressure should be made the fluid intake and urine output recorded and the urine examined for specific gravity albumin and blood Microscopic examination of the deposit for red cells leucocytes and casts should be made twice weekly Renal function te ts and plasma protein examination should be made It is important to search for any residual primary infection such as tonsillitis and to treat such infection with the appropriate dose of penicillin according to age In this way it may be hoped to avoid recrudescences which may otherwise lead to serious relapse of nephritis during the recovery period A low protein low salt high carbohydrate diet should be given to minimise protein breakdown and sodium retention In children and in co operative adults this can be very simply provided by restricting the fluid intake to 1 or 2 pints of orange juice daily with a carbohydrate diet until the acute stage of the disease has passed Diuretics and particularly potassium salts should not be given The patient must be kept in bed until pitting œdema has disappeared the blood pressure has returned to normal and the urine is free of albumin If after a period of at least 4 weeks from the onset the only residual urinary abnormalities are a faint trace of albumin and a few red cells per high power field on microscopic examination of the deposit the patient may be allowed up but periodic examination of the urine deposit for erythrocytes is advisable until these disappear in children particularly adolescents this may take up to 12 months Tonsillectomy is not advised until the nephritis has resolved and should then only be undertaken if the tonsils are obviously chronically inflamed or there is a past history of repeated sore throats

Complications —Secondary infection should be treated with an appropriate antibacterial agent penicillin being the most useful Heart failure is a definite risk when there is marked hypertension In severe cases with acute pulmonary œdema venesection is the treatment of choice If the blood pressure is very high reduction with hexamethonium salts may be worthy of trial although experience in this connection is still limited Digitalis is of questionable value and in the majority of patients spontaneous improvement occurs as the nephritis subsides The most serious complication is anuria If this persists uræmia rapidly develops and may be complicated by extrarenal nitrogen retention due to vomiting The essence of treatment is to maintain the electrolyte and fluid balance keeping a careful watch on the serum potassium as described under the treatment of traumatic anuria No attempts should be made to force diuresis by intravenous infusions and potassium salts should never be administered

Hypertensive encephalopathy occurs with about the same frequency as heart failure in patients with very high blood pressure Recent experimental work indicates that the syndrome is due to cerebral vascular spasm and in the later stages this may lead to cerebral œdema Prompt venesection with removal of 1 pint of blood will sometimes produce dramatic improvement Failing this attempts should be made to reduce the blood pressure by intramuscular injection of hexamethonium salts The cerebrospinal fluid pressure is not usually raised in the early stages but lumbar puncture should be carried out and if the pressure is high an intravenous injection of 100 ml 50 per cent sucrose solution should be given in an attempt to reduce cerebral œdema Alternatively 4 to 6 oz 25 per cent magnesium sulphate may be given per rectum but this is a less effective measure Hypertensive encephalopathy and heart failure may occur together but fortunately reduction of the blood pressure

will usually relieve both conditions There is often a slight to moderate degree of anæmia in acute nephritis probably due to the initial streptococcal infection and it should be adequately treated by iron preparations

Rapidly progressive course—In these patients the nephritis is severe and hæmaturia hypertension and œdema persist Treatment is continued as in the acute stage, and complications such as heart failure and hypertensive encephalopathy should be dealt with promptly The patient should be kept at rest in bed for at least 3 months since complete recovery may occur even after this prolonged course Diuretics must not be given nor fluids restricted if renal failure is present Tonsillectomy is to be avoided as it may aggravate the nephritis in this active stage

Slowly progressive course (chronic Type 1 nephritis)—In the long intermediate stage before the development of renal failure and severe hypertension it is most important that the patient should not be made an invalid by unnecessary or even harmful treatment There are frequently no symptoms during this time, the only findings being residual albuminuria and perhaps slight variable hypertension The old practice of protein starvation is thoroughly bad as it leads to protein deficiency iron deficiency anæmia, malnutrition and the conviction of invalidism A normal *diet should therefore be allowed so long as the renal function tests are normal* Iron should be prescribed if there is any degree of anæmia and the only necessary medical attention is a periodic examination at 3 to 6 monthly intervals when the urine and blood pressure should be tested and renal function tests occasionally carried out. In the later stages the blood pressure tends to rise progressively and renal impairment develops Headache and breathlessness may be presenting symptoms and should be treated as in benign hypertension When other analgesics fail, ergotamine tartrate sometimes relieves hypertensive headaches, especially if these are migrainous in character If left ventricular failure is severe rest in bed digitalis and mercurial diuretics are indicated The appearance of retinopathy probably justifies an attempt to reduce the blood pressure by hexamethonium derivatives When renal impairment appears, the fluid intake should under no circumstances be restricted protein in the diet should be reduced only when the blood urea rises considerably above the normal *e g to 100 mg per cent*

Anæmia should be treated by iron preparations, but when uræmia is present the anæmia is usually refractory and the only beneficial treatment is blood transfusion It is well to remember that some degree of uræmia may be due to heart failure or anæmia or even to severe hypertensive crises and some improvement may be expected if these complications are adequately treated

TYPE 2 NEPHRITIS

Synonyms—Subacute and Chronic Parenchymatous Nephritis Nephrotic Nephritis *Hydropigenous Nephritis Lipoid Nephrosis*

Type 2 nephritis is less common than Type 1 nephritis but its incidence ranks high in a clinic for renal diseases since in the majority of patients it follows a chronic course of many years duration The incidence is more uniformly distributed over the first six decades of life than that of Type 1 nephritis In young children and occasionally in adults hypertension and hæmaturia may be absent so that the condition is indistinguishable from so called lipoid nephrosis Long term clinical and histological study of such cases reveals however no clear demarcation from Type 2 nephritis and it would seem reasonable in the great majority of instances to regard lipoid nephrosis as a mild form of the latter

Ætiology—In most cases no ætiological factor is established and it is unusual to obtain a previous history of acute streptococcal infection This is no doubt partly due to the fact that albuminuria (and therefore the onset of disease) may precede the onset of œdema by months or years The development of œdema which in most cases first brings the patient to the doctor may be precipitated by severe *intercurrent*

infection or by pregnancy the common factor presumably being a lowering of the plasma protiens which upsets the balance between loss of protein in the urine and new protein formation

Pathology—The kidney is large and pale and may or may not be œdematous The kidney pattern and the demarcation of cortex from medulla are blurred, and fatty changes in the tubules and *interstitial tissue may appear as white streaks on the cut* surface The microscopic picture depends on the stage of the disease and the severity In cases with little or no hypertension the picture resembles that described in nephrosis *i e* there are minimal changes in the glomeruli consisting of bland focal necroses together with deposition of lipoid in the tubular epithelium and interstitial tissue, slight interstitial cellular infiltration may be present In more severe cases there is a diffuse proliferative glomerulitis with accentuated lobulation of the tufts and swelling of the capillary basement membrane As this lesion progresses deposits of hyaline material appear in the glomerular tufts and the glomerular capsule undergoes fibrous thickening but epithelial crescent formation is almost always absent Glomerular hyalinisation gradually and very slowly increases so that even after 10 years the characteristic glomerular lesion may still be recognisable The tubules undergo fairly diffuse atrophy and a uniform interstitial fibrosis develops but it is unusual for more than a moderate degree of renal contraction to result Vascular lesions are not conspicuous although occasional arteriolar necroses may be observed in those cases with a malignant hypertensive termination

Symptoms—It has already been stated that albuminuria discovered on routine examination may provide the first indication of the disease months or years before the appearance of œdema or other symptoms In most patients however Type 2 nephritis presents with gradual or rapid onset of œdema, which steadily increases and tends to become massive The œdema may be generalised, affecting the face hands trunk and legs It is often first noticed as puffiness of the eyelids or it may first appear as a swelling of the feet and ankles extending up the legs The patient may feel quite well apart from the disability caused by œdema On the other hand there is more usually complaint of malaise and fatigue, loss of appetite and nausea and sometimes of epigastric pain There may be cough and slight shortness of breath due to slight bronchial catarrh œdema of the lungs or hydrothorax A pericardial effusion may develop Swelling of the abdomen may be the result of œdema of the abdominal wall or ascites The face is pale and the eyelids and cheeks are puffy, but the mucous membranes are of a good colour and the blood count is usually normal The urine is reduced in quantity its specific gravity is normal it contains a large amount of albumin often amounting to 0 5 or even 1 per cent and readings of 4 per cent or even more have been recorded In mild cases the urinary deposit contains only a slight excess of cells and few or no casts while red blood corpuscles are generally absent In the more severe cases leucocytes red blood cells and granular casts are regularly found in the urine deposit The blood pressure may be normal or moderately raised There is no retinitis in the early stages Characteristic changes are found *in the blood* The plasma *albumin falls more considerably than in other* forms of Bright s disease Approximate normal figures are plasma albumin 4 g per cent globulin 2 5 g per cent, total protein 6 5 g per cent which gives an albumin globulin ratio of 1 6 to 1 In Type 2 nephritis plasma albumin may be 1 to 2 g per cent globulin 2 5 to 3 5 g per cent so that albumin globulin ratio is often less than unity The blood cholesterol may be 300 to 800 mg per cent (normal 130 to 250 mg per cent) The blood urea is often raised especially in patients with gross œdema and oliguria but concentration tests are unimpaired

Complications—These are

(1) Pulmonary œdema and cerebral œdema which occur only in cases with gross anasarca Cerebral œdema is very rare but has been observed in children after rapid generalised increase in swelling

(2) Pyogenic infection—the common ones being pneumococcal peritonitis pneumonia and erysipelas

(3) Hypertensive encephalopathy Owing to the moderate degree of blood pressure elevation this complication is not often seen but it may develop in the subacute stage when, especially in adult males, severe hypertension is sometimes encountered. The symptoms are identical with those described under Type 1 nephritis

Diagnosis—The insidious onset with œdema gross albuminuria and hypoproteinæmia is so characteristic of Type 2 nephritis that there is usually no problem of diagnosis There may be some difficulty in the early stages in distinguishing it from Type 1 nephritis running the rapidly progressive course Here also there is often gross generalised œdema and heavy albuminuria but the acute onset and greater depth of hæmaturia hypertension and renal impairment enable the separation to be made in most cases Amyloid disease of the kidney also produces generalised œdema albuminuria and hypoproteinæmia Some obvious primary infection such as bronchiectasis, osteomyelitis or tertiary syphilis is usually present the spleen may be enlarged and the Congo Red test is of particular value The nephrotic syndrome occasionally arises in the later stages of diabetic glomerulosclerosis Although Type 2 nephritis may occur in the diabetic the appearance of œdema and albuminuria in the course of chronic diabetes is usually due to this specific form of glomerular hyalinisation Disseminated lupus erythematosus may produce a glomerulo nephritis in which swelling of the capillary basement membrane resembles that seen in some cases of Type 2 nephritis and clinically the nephrotic picture may develop The associated features of disseminated lupus are however diagnostic Another rare cause of generalised œdema with gross albuminuria is bilateral renal vein thrombosis but, as a rule this diagnosis is only made post mortem It is possible that the nephrotic syndrome may arise from other causes including chemical poisons and secondary syphilis, cases of obscure origin have been described in several members of the same family

Course and Prognosis—Complete recovery is rare in Type 2 nephritis particularly in adults Clinical resolution does however, occasionally occur, sometimes after many years of persistent or recurrent œdema In children, recovery is not uncommon particularly when the features are those of nephrosis *i e* when hypertension and hæmaturia are absent In the great majority of patients however the disease runs a steadily progressive course and the prognosis is closely related to the degree of hypertension which develops With no hypertension or a moderate degree which subsides under treatment, good health often continues for many years whereas with marked elevation of blood pressure the course may be rapidly progressive Hypertension is generally more severe, and the course correspondingly shorter in men than in women Thus in men Type 2 nephritis usually continues with variable œdema moderate hypertension and considerable albuminuria after 2 or 3 years progressive renal impairment sets in and leads to uræmia 3 to 5 years from the onset of œdema often with the development of the malignant hypertension syndrome In less severe cases (more commonly women) the disease runs a slower course œdema may subside very gradually over the course of months or may recur at intervals but in the absence of hypertension the patient may lead a useful and symptom free existence for 10 or 20 years In this group the degree of albuminuria tends to diminish and the plasma proteins to rise at a variable interval after the onset Intercurrent infection may occur at any time and this is particularly serious in children with generalised œdema the common infections being pneumococcal peritonitis *pneumonia or erysipelas* Occasionally intercurrent infection is associated with an exacerbation of the nephritis and there may be frank hæmaturia during such episodes in other patients infection may precipitate a massive diuresis with subsequent reduction in the degree of albuminuria

Treatment—In the early stages particularly if examination of the urinary deposit

reveals evidence of active nephritis (i e red cells leucocytes and granular casts) treatment should follow the regime advised in acute Type 1 nephritis As a rule however the disease is in its subacute or chronic stage when the patient is first seen Even then it is advisable to insist on rest in bed so that a full assessment of the condition can be obtained Observations on the blood pressure urine renal function and plasma proteins should be made as in Type 1 nephritis and it is of value to record the patient s weight daily as this gives a useful index of changes in œdema The objectives are to rest the patient treat or prevent secondary infection counteract plasma protein depletion by a high protein diet and encourage the removal of œdema fluid Very severe generalised œdema may present an urgent problem since particularly in children fatal pulmonary œdema or cerebral œdema may result In the average case however no heroic measures are required and since the œdema is a manifestation of nephritis it cannot be expected to resolve completely until the nephritis subsides It is wise therefore to maintain complete rest and during the first week or two treatment should consist in restriction of salt intake the sodium content of the food being reduced to 0 5 g daily The diet should otherwise be adapted to please the patient Under this regime œdema will gradually diminish in most instances Rest in bed should be continued so long as red blood cells and leucocytes persist in the urine Heavy proteinuria may continue for many months after the first few weeks therefore and when œdema is no longer severe it is wise to give a high protein diet (up to 200 g daily) in an attempt to restore the depleted body protein No considerable rise in plasma proteins must be expected for 1 or 2 months or even longer If the above treatment does not succeed in reducing œdema mercurial diuretics should be given intramuscularly (Mersalyl 1 to 2 ml) twice or three times weekly at the start and once a week subsequently If the diuretic response is poor ammonium chloride may be given before the injection If salt restriction and mercurial diuretics both fail to promote diuresis acu puncture of the legs under cover of adequate doses of penicillin will always produce an effective reduction in œdema The patient should be placed in Fowler s position before this is carried out to allow the œdema fluid to gravitate to the legs When subcutaneous drainage is under way it may be found that mercurial diuretics will now produce a better response If as is frequently the case ascites and pleural effusions are present paracentesis may be necessary and again mercurial diuretics may give an improved response after this has been performed It is a common observation that massive diuresis may occur in refractory cases after an infection such as measles or pneumonia Attempts to reproduce such a response has therefore been made by T A B injections or even malaria therapy but the results are not impressive and the use of direct subcutaneous drainage under antibiotic cover has made this rather drastic therapy unnecessary

Complications —Pulmonary œdema and the much rarer complication of cerebral œdema occur only when subcutaneous swelling is gross and both should be avoidable if the measures outlined above are employed in good time Should either of these complications develop direct subcutaneous drainage should be started immediately Infections such as pneumonia pneumococcal peritonitis or erysipelas should be treated by appropriate doses of penicillin In the subacute stage of the disease hypertensive encephalopathy occasionally occurs in the rare case with severe hypertension and should be treated as in acute nephritis Iron preparations should be given if anæmia develops

Chronic Type 2 nephritis —After the initial stage continued supervision is necessary When the patient first becomes ambulant it is common for some œdema of the legs to return and this can usually be controlled by fitting full length elastic stockings which should be worn only during the day In some cases œdema continues for many months and can only be satisfactorily controlled by weekly or twice weekly injections of mercurial diuretics The *high protein low salt diet should be continued* ,

salt free bread and a substitute for table salt which does not contain sodium can now be purchased Iron should be prescribed for anæmia and any devices which may improve the patient's sense of well being, including a stimulating tonic alcohol in moderation or a seaside holiday are to be commended The main point, however, is to encourage the patient to lead a normal life and return to work, with the obvious precautions of avoiding chills and excesses of any kind It is in the nature of the disease that relapses tend to occur If these are mild, and unaccompanied by more than slight œdema, rest in bed at home is often sufficient, but if œdema increases the patient should be admitted to hospital and treated as described above In the later stages of the disease when hypertension and uræmia develop, treatment is the same as in chronic Type 1 nephritis

RENAL VASCULAR DISEASE

BENIGN ESSENTIAL HYPERTENSION

Synonym —Benign Nephrosclerosis

In this form of hypertension, renal vascular changes rarely produce clinical symptoms, the disorder being one of chronic arterial and arteriolar degeneration, and it will be necessary to make only a brief reference to it here

Pathology —The chief kidney changes are in the smaller arteries and arterioles They are described in detail on p 909 In contrast with malignant nephrosclerosis there is only hyaline and fatty degeneration of the arterioles There may be renal ischæmia and consequent irregular contraction and fibrosis of the renal parenchyma. In some cases this condition is marked and a granular contracted kidney results There is then a patchy fibrosis of glomeruli with tubular atrophy and secondary interstitial changes This fibrotic atrophy is secondary to the arterial narrowing and it is because of its patchy distribution that renal function is not impaired

Symptoms —See Benign Essential Hypertension (p 909) In some cases the urine contains a trace of albumin but this is confined to long standing cases with severe ischæmic fibrosis Given this clinical picture the differential diagnosis from chronic nephritis is made on the absence of a past history of acute nephritis and of renal failure There are occasional cases presenting with the clinical features of benign hypertension in which intravenous pyelography reveals unilateral renal disease If this is discovered in childhood or early adult life removal of the diseased kidney may be followed by recovery from the hypertension In a small proportion of cases (probably not more than 5 per cent) benign hypertension may progress to malignant hypertension and terminate in uræmia

Treatment —See that of Hypertension (p 911) the Heart in Hypertension (p 851) and Uræmia

MALIGNANT ESSENTIAL HYPERTENSION

Synonym —Malignant Nephrosclerosis

As in benign hypertension the renal changes are secondary to the vascular lesions This disease is called malignant nephrosclerosis because the kidneys are severely affected so severely in fact that fatal uræmia is the usual outcome

Pathology —The chief kidney changes are in the smaller arteries and arterioles They are described on p 913 In contrast with benign nephrosclerosis, there is in addition, fibrinous necrosis especially of the arterioles

Symptoms —These are described on p 914

Diagnosis —The differential diagnosis of malignant nephrosclerosis from chronic nephritis depends on the fact that in the former there is no past history of acute or chronic nephritis, nor is there renal œdema Further, in malignant nephrosclerosis

papillœdema usually appears whilst renal function is fairly good in fact it may be normal and there may be no albuminuria In chronic nephritis however, renal failure is usually advanced by the time papillœdema develops

Treatment—See that of Hypertension (p 911) the Heart in Hypertension (p 851) and Chronic *Uræmia (p 1122)*

NEPHROSCLEROSIS WITHOUT HYPERTENSION

Synonym—Senile or Atheromatous Kidney

In this form of kidney disease also the vascular changes are *of greater importance* than the renal and it is only necessary to deal briefly with the affection

Pathology—The kidneys show depressed red areas which are due to contraction of fibrous tissue along the distribution of particular interlobular arteries and therefore tend to be conical in form with their base to the surface of the organ There is an *absence of* cardiac hypertrophy The *glomeruli in scarred areas shrink*, and the connective tissue around them becomes condensed and thickened The degenerate glomerulus and its capsule fuse together and undergo fatty and fibrotic changes The atheromatous kidney is, therefore contracted due to atrophy following insufficient circulation with consequent fibrosis

Symptoms and Diagnosis—*There may be gradual failure of the physical and* mental powers—described by Allbutt as contraction of the spheres of bodily and mental activity —rather than the more dramatic events of malignant nephro sclerosis There is a trace or more of albumin in the urine The radial artery is thickened and tortuous The blood pressure is not high and there is an absence of cardiac hypertrophy Death by cardiac failure or intercurrent affections is the commonest ending while cerebral hæmorrhage and uræmia are unlikely

RENAL LESIONS IN DIABETES

Renal disease is now one of the commonest fatal complications of diabetes This is due to the fact that control of hyperglycæmia and ketosis by insulin has greatly *prolonged life so that the vascular complications are becoming increasingly prominent* The gradual change in the natural history of diabetes over the past 20 years has brought to light a specific form of renal involvement which is closely related to chronic vascular degeneration in other organs This condition first described by Kimmelstiel and Wilson in 1936 and named by them *intercapillary glomerulosclerosis is the commonest renal lesion in diabetes* Secondly *ischæmic* atrophy of the kidney tends to be very severe in the diabetic thirdly ascending pyelonephritis may occur in a particularly intense form leading to medullary necrosis The diabetic patient is therefore particularly liable to these three forms of renal damage In addition other types of renal disease such as glomerulo nephritis are occasionally encountered

DIABETIC GLOMERULOSCLEROSIS

Incidence—It is probable that diabetic glomerulosclerosis occurs in 10 to 20 per cent of all cases In long standing diabetes starting before the age of 15 the incidence is much higher and may reach 50 per cent Its occurrence is related to long duration of diabetes rather than to the age of the patient. Although it may be discovered within a few years of the onset of glycosuria the average duration of diabetes when the renal lesion first appears is about 10 years Thus the majority of patients first present evidence of this renal disorder in middle age The incidence is higher in females than in males Neither *severity of diabetes nor insulin* treatment play any essential role in its pathogenesis since the lesion is found in patients who have never received insulin and it is not uncommon in those who have a mild easily

controlled diabetes with little or no tendency to ketosis It would thus appear that as with the other vascular complications of the disease there is little relation between the incidence and severity of diabetic glomerulosclerosis on the one hand and the disturbance of carbohydrate metabolism on the other Apart from these factors nothing is known about the ætiology of the process

Pathology—As its name implies diabetic glomerulosclerosis consists of a degeneration of the glomerular tuft This takes the form of progressive hyalinisation but it is possible to recognise several distinct histological features The first is a nodular deposit of hyaline material in the glomerular tuft which resembles amyloid material but does not take amyloid stains this lesion is peculiar to diabetes In addition the majority of affected glomeruli show a diffuse hyaline change which is seen to be an extension into the glomerular tufts of a similar hyaline degeneration in the afferent arterioles An identical but much less conspicuous hyaline degeneration may result from senile atherosclerosis of the kidney Thirdly lipo hyaline deposits and occasional capillary aneurysms occur within the glomerular tuft and contribute to its disorganisation, focal glomerular necroses may also be found particularly if the blood pressure has been very high It will be seen therefore that diabetic glomerulosclerosis is closely associated with severe degenerative changes in the arterial system of the kidney furthermore the association is equally close with severe atheromatous change elsewhere in the body especially in the heart brain and retina Because of the severe ischæmic atrophy the kidney is usually considerably contracted and the arteries are seen to be extremely prominent

Clinical Features—Albuminuria may for a period of many years be the only manifestation of diabetic glomerulosclerosis It is variable in amount and is not usually accompanied by inflammatory elements in the urinary deposit The further development of the clinical syndrome is due not so much to the specific diabetic lesion but to other complications resulting from generalised arterial degeneration Hypertension heart failure and progressive ischæmic damage to the kidney are the most important of these Impairment of renal function is the rule although its development is very gradual In the later stages albuminuria increases to a degree which leads to a considerable reduction in the plasma protein level When this occurs and particularly when myocardial failure due to coronary disease supervenes severe generalised œdema may appear Hypertension is usually, but not invariably present and is moderate in degree malignant hypertension is only rarely encountered The final picture is one of combined heart failure and renal failure and there is often severe mental disturbance due to cerebral vascular degeneration Diabetic retinopathy will be found in practically all patients with diabetic glomerulosclerosis and diabetic peripheral neuritis usually mild in degree, is also commonly present During the later stages of the disease it is not infrequently found that the insulin requirement falls This is probably accounted for by the diminished food intake and restricted activity of the patient due to increasing incapacity

Diagnosis—When the usual investigations have excluded focal lesions such as calculus tuberculosis neoplasm cystitis and pyelitis chronic albuminuria in a diabetic patient is almost certainly due to intercapillary glomerulosclerosis with associated renal ischæmic damage The presence of retinopathy strongly supports the diagnosis as does evidence of arterial degeneration in other organs There is no specific test for the disease The association with retinopathy is so close that if renal failure is discovered in a diabetic patient in the absence of retinal changes it is highly probable that some other form of kidney disease is the cause

Prognosis—As already indicated glomerular hyalinisation and ischæmic atrophy develop very slowly and albuminuria may be present for 10 years before the late complications supervene The prognosis in fact depends rather more on the extent of vascular degeneration elsewhere in the body than on the presence of glomerulosclerosis

Treatment—Apart from control of the diabetes treatment is the same as in other patients with chronic hypertensive renal disease (see Chronic Nephritis p 1122)

ACUTE MEDULLARY NECROSIS

This is a severe suppurative pyelonephritis which leads to zonal necrosis of the renal medulla

Pathology—This is the same as in pyelonephritis except that necrosis of parenchymal tissue occurs and multiple small abscesses may be formed Severe active pyelitis is present The necrosis is obvious to the naked eye as yellowish white areas lying between the base of the renal pyramid and its papilla There may be multiple necroses in different pyramids and one or both kidneys may be involved Intercapillary glomerulosclerosis is sometimes associated with medullary necrosis

Symptoms—The symptoms may be those of acute pyelitis but more commonly the condition will be found in an elderly patient who becomes severely ill and is found in what appears to be diabetic coma The condition should indeed be suspected in any patient especially a woman who fails to recover from coma after diabetic ketosis is controlled In such circumstances the urine should be examined for pus and organisms Renal calculus or urinary obstruction may be the underlying cause of ascending infection Unless the condition responds to treatment oliguria develops and death occurs in uræmia

Treatment—Prophylaxis consists in dealing with renal calculi or any obstructive lesion of the renal tract which may be discovered in the diabetic patient The presence of pyuria in a severely ill or comatose diabetic calls for prompt and effective antibiotic therapy Sensitivity tests should be carried out on the organisms cultured from the urine and streptomycin chloramphenicol or oxytetracycline should be given according to the results General therapeutic measures are the same as for acute pyelitis

THE CONTRACTED KIDNEY

In the past various terms have been applied to the contracted kidney but the ætiology and natural history of the process have often been obscure Contraction of the kidney is due to destruction of nephrons and the development of interstitial fibrosis It will be obvious from the conditions already discussed that these changes may arise in many ways nevertheless there may be no previous history of renal disease The clinical manifestations are those of renal failure and there are often no distinguishing features to indicate the nature of the primary lesion The following are the common causes of contracted kidney

CHRONIC TYPE 1 NEPHRITIS—Some of the smallest contracted kidneys result from the slowly progressive course of Type 1 nephritis The disease may have been present for 30 or 40 years and in about half the cases there is no history of acute nephritis The renal contraction is due to a combination of the original nephritis and of subsequent hypertensive damage The former produces diffuse fibrosis and the latter focal scarring The number of surviving nephrons may be extremely small so that only occasional hypertrophied glomeruli with greatly dilated tubules are seen in each low power field

CHRONIC TYPE 2 NEPHRITIS—Renal contraction in this form of Bright s disease is usually only slight or moderate and is limited to those cases which run a slow course of 10 to 20 years Renal failure is slow in development and may be present as long as 5 years before symptoms of uræmia appear A malignant hypertensive termination is common in these cases

CHRONIC PYELONEPHRITIS—Some of the most contracted kidneys fall into this group Broad zones of interstitial scarring lead to a coarse irregularity of the kidney Contraction often affects the two kidneys unevenly and one kidney may be reduced

to a fibrous remnant whilst the other is greatly hypertrophied In such cases of unilateral renal disease severe hypertension may be present and may progress to a malignant termination The hypertrophied kidney may then show the characteristic histological changes of malignant nephrosclerosis

CONGENITAL RENAL LESIONS —Here again the kidneys may be extremely small due to a failure of development (hypoplasia) as well as to fibrotic contraction usually attributable to ascending pyelonephritis This ascending contraction ' is particularly prominent in cases of idiopathic dilatation of the renal tract An unexplained feature of congenitally small kidneys (described by Rose Bradford) is the absence of associated hypertension and cardio vascular hypertrophy Nevertheless severe hypertension occasionally occurs

MALIGNANT ESSENTIAL HYPERTENSION —As a rule the kidneys are not contracted in this disorder owing to the rapidly progressive course Occasionally, however, and particularly in older subjects the disease may progress relatively slowly over the course of 3 or 4 years There is often in these patients a preceding history of long standing benign hypertension and a moderate to severe degree of renal contraction takes place

BENIGN ESSENTIAL HYPERTENSION —Renal contraction in this disorder is unusual but is seen in moderate degree when atheroma of the renal arteries is severe The mechanism of contraction only differs from that of the senile arteriosclerotic kidney in the more extensive fatty hyaline degeneration of the arterioles, which gives a finely granular appearance to the surface due to subcapsular scarring Obstruction of one renal artery by an atheromatous plaque may reduce the affected kidney to a fibrous remnant and this is one of the unilateral lesions which may lead to hypertension In diabetes arterial degeneration is severe in the kidney, as in other organs and some contraction of the kidney is likely This will be all the greater if diabetic glomerulo sclerosis is also present

HYDRONEPHROSIS —Obstructive lesions of any kind lead to pressure atrophy of the renal parenchyma and the renal substance may be reduced to a thin layer of fibrotic tissue surrounding the hydronephrotic sac Where chronic ascending infection has been present in the early stages as in many cases of renal calculus, the kidney may be small and contracted with a minor degree of hydronephrosis

TRAUMATIC ANURIA AND ALLIED CONDITIONS

Synonyms —Acute Cortical Ischæmia, Acute Tubular Necrosis Lower Nephron Nephrosis Crush Kidney Acute Focal Interstitial Nephritis

The clinical manifestations and renal histological changes in this disorder were first adequately studied in patients who received crushing injuries to the limbs during air raids on London in the War of 1939–1945 The characteristic clinical feature is suppression of urine and little structural damage may be found in the kidney except for focal areas of tubular necrosis Since its first description the syndrome has been recognised as a sequel of a variety of widely differing ætiological factors Apart from crushing injuries it may follow prolonged application of tourniquet to a limb, any form of major surgical trauma especially gall bladder operations obstetric shock retroplacental hæmorrhage infected abortion other severe infections such as Weil s disease and blackwater fever incompatible blood transfusion sulphonamide therapy and perhaps acute poisoning with heavy metals such as mercury and bismuth

Pathology —There is a severe dysfunction of the whole nephron glomerular filtration being inhibited or grossly diminished whilst tubular reabsorption is in abeyance Histologically the only findings are occasional foci of epithelial necrosis in the distal convoluted tubules associated with slight inflammatory infiltration Blood pigment casts may be present in the tubules

Symptoms —Suppression of urine is the primary disorder and this leads to acute uræmia with vomiting, drowsiness muscular twitching and coma Purpura

may appear hypertension is slight or absent but may develop in the later stages during recovery Restoration of renal function may occur after severe oliguria lasting up to 3 weeks If the patient survives the acute stage copious polyuria develops This may however give a false impression of recovery of renal function for the urine at first approximates in composition to glomerular filtrate Since tubular reabsorption is in abeyance an output of many litres of urine may therefore correspond to only a fractional recovery of glomerular filtration and the blood urea may still continue to rise There is a danger in this stage of excessive electrolyte depletion due to failure of tubular reabsorption restoration of tubular concentrating power may not be complete for many months

Treatment—During the stages of anuria and subsequent polyuria it is essential to maintain electrolyte and fluid balance since over hydration in the anuric stage carries a grave risk of fatal pulmonary œdema Electrolyte depletion due to lack of tubular reabsorption in the polyuric stage can be equally serious Endogenous protein breakdown leads to accumulation of extracellular potassium in the absence of urinary excretion and if this is excessive death may occur from cardiac arrest Potassium salts must therefore under no circumstances be administered at this stage Protein breakdown can be reduced by high carbohydrate diet and the extracellular potassium can if necessary be reduced by intravenous insulin or sodium loaded ion exchange resin The following regime of treatment should be followed 1 litre of 40 per cent glucose is given daily by intra gastric drip If any urine is passed an equal volume of extra water is added If vomiting occurs saline solution equivalent to that lost in the vomit is added If vomiting persists oral treatment is discontinued and 1 litre of 40 per cent. glucose is given intravenously by catheter via the saphenous vein into the inferior vena cava Half a million units of penicillin should be given daily intra muscularly A rise of serum potassium above 6 m Eq/litre may be dealt with in the first instance by the injection of insulin two to three times daily when the blood sugar is above normal If the rise in serum potassium continues sodium sulphonic ion exchange resin should be given orally (15 g t d s) or if this cannot be tolerated 30 g daily per rectum This form of conservative treatment has replaced the use of the artificial kidney In the stage of polyuria sodium depletion may occur so that the fluid and electrolyte intake must be increased to compensate for the amount lost in the urine

TOXIC NEPHROSIS AND RELATED DEGENERATIVE RENAL LESIONS

The term nephrosis means tubular epithelial degeneration consequently many unrelated conditions are included under this heading The types of tubular degeneration are albuminous lipoid hyaline droplet and necrotising or fibrinoid Amyloid nephrosis is a special type which is dealt with elsewhere (p 1131) Lipoid nephrosis has already been described under Type 2 nephritis and one form of necrotising nephrosis has been dealt with under Traumatic Anuria

Simple Nephrosis in which there is albuminous degeneration of the tubular epithelium occurs in febrile states and toxæmias From the renal point of view it is of no clinical significance except that mild albuminuria results Sometimes heavy albuminuria is produced for example in hepatic failure due to acute yellow atrophy or Weil s disease nitrogen retention may develop in such patients but is probably extrarenal in origin The term hepato renal syndrome has no specific meaning but is sometimes used for this combination of liver disease and renal tubular nephrosis

Mercurial Nephrosis is a typical example of severe tubular degeneration associated with chemical poisoning Ingestion of mercuric salts or even therapeutic use of mercurial lotions may in patients with idiosyncrasy produce fatty hyaline droplet and fibrinoid necrosis of the tubular epithelium which later *undergoes calcification*

Oliguria and hæmaturia are produced, along with other manifestations of mercurial intoxication and fatal uræmia may result In its clinical course and possibly in the development of the lesion this type of nephrosis is allied to that occurring in traumatic anuria There is some evidence that organic mercurial diuretics may damage the renal tubules, but it is extremely rare Bismuth poisoning may produce a similar picture to mercurial nephrosis but the renal damage is less severe Other chemical poisons which affect the kidney are carbon tetrachloride and phosphorus, they cause severe fatty degeneration of the tubules but the whole nephron is probably affected since fatal uræmia may occur

ECLAMPTIC NEPHROSIS —In fatal eclampsia severe tubular damage including fatty and hyaline droplet degeneration is found post mortem Although this is referred to as a 'toxæmia of pregnancy" it is more probable that the lesion is an acute ischæmic one comparable to that seen in malignant hypertension or traumatic anuria These changes like other tubular degenerative lesions, are difficult to relate to the clinical features and it is doubtful whether chronic renal damage results from this form of nephrosis Persistent hypertension and albuminuria following so called toxæmia of pregnancy usually indicate pre existing renal disease or hypertension Any effect cyesis may have on the course of these disorders is probably due to exacerbation of the hypertension which so frequently occurs about the middle of pregnancy

BILATERAL CORTICAL NECROSIS is a rare renal complication of pregnancy Although it occasionally occurs in male subjects without any obvious cause it may result from chemical poisoning or severe infections such as malaria In pregnancy it is usually associated with eclampsia or retro placental hæmorrhage Its pathogenesis is probably related to that of acute tubular necrosis (traumatic anuria) The clinical picture is one of severe abdominal pain and anuria leading to rapidly fatal uræmia without hypertension

OTHER FORMS OF NEPHROSIS —Tubular degeneration occurs in gout secondary to deposits of sodium biurate crystals in the interstitial tissue The common renal complication of gout is however, a chronic 'interstitial nephritis' probably due to associated essential hypertension

Myelomatosis is not infrequently complicated by severe renal damage The picture is often a mixed one due to ascending nephritis or ischæmic changes There is however a specific lesion in myelomatosis consisting of tubular atrophy consequent on the formation of obstructive casts which are in some way related to Bence Jones protein The glomeruli in such kidneys may be remarkably normal

NEPHROCALCINOSIS —It has already been stated that calcification of the tubular epithelium may follow necrotic changes such as result from mercury poisoning Similar epithelial calcification may be a late sequel of alkalosis due to severe vomiting or may follow traumatic anuria sulphonamide anuria and myelomatosis An entirely different type of nephrocalcinosis so called metastatic calcification occurs in hyper parathyroidism large interstitial deposits being formed Still another form is that occurring in hyperchloræmic acidosis in children in which the primary defect is a failure of the proximal tubule to reabsorb bicarbonate

CONGENITAL ABNORMALITIES OF THE KIDNEY

Many errors of development resulting in abnormalities of the shape or position of otherwise normal kidneys are of little clinical importance They are unlikely to give rise to symptoms or to progressive renal impairment although there is evidence that such kidneys have an increased tendency to infection Maldevelopment of the kidneys leading to insufficient functioning nephrons may without added infection lead to renal failure The pathological differentiation of such kidneys from those which are contracted as a result of chronic atrophic pyelonephritis or of vascular or ureteric occlusion early in life, may be extremely difficult if not impossible The

recognition of a congenitally absent or insufficient kidney is essential when nephrectomy is being considered as treatment of disease in the opposite kidney

RENAL AGENESIA —Agenesia implies the complete absence of a kidney Bilateral agenesia is of course incompatible with survival

RENAL APLASIA —An aplastic kidney contains no renal tissue capable of normal function Glomerular and tubular elements are contained perhaps with cysts within a dense stroma of fibrous tissue and scanty smooth muscle and the ureter is often not patent Owing to the difficulty of distinguishing such anomalous structures from secondarily contracted kidneys there is a lack of evidence whether they can be responsible for the development of hypertension

RENAL HYPOPLASIA —Truly hypoplastic kidneys contain virtually normal nephrons in markedly reduced numbers They are miniatures with reduced function commensurate with their size and are therefore unable to maintain life indefinitely if the condition is bilateral The renal failure which develops is analogous to that occurring in experimental animals in which a large part of the renal tissue has been removed Histologically hypertrophy of the individual nephrons and tubular dilatation are found

Hypoplasia may be one cause of the so called Rose Bradford kidneys in children or young adults pyelonephritis or glomerulo nephritis contributing to the picture of gross renal contraction in which areas of hypertrophied elements alternate with dense interstitial fibrosis A closely related group of very contracted kidneys is characterised by idiopathic dilatation of the urinary tract The condition may be unilateral or bilateral and the bladder may be dilated No organic cause of obstruction is found in the majority of these cases but chronic pyelonephritis is an invariable complication It is possible also that Rose Bradford kidneys may result from ascending infection of normal kidneys in early childhood or *in utero* In all these groups of gross renal contraction renal failure is prolonged and the symptoms of polyuria and polydipsia are particularly prominent Osteodystrophy (renal rickets and dwarfism) may occur in association with phosphate retention acidosis parathyroid hyperplasia and metastatic calcification Hypertension is infrequent whilst very occasionally hypotension is associated with sodium depletion due to chronic acidosis

CONGENITAL POLYCYSTIC DISEASE —This condition is described on p 1146

LARDACEOUS DISEASE

Synonyms —Amyloid or Waxy Kidney

Definition —A pathological condition in which the blood vessels of the kidney and in more advanced cases the tunica of the tubules and the interstitial tissue also are the seat of waxy degeneration

Ætiology —This affection is now rarely met with It attacks men more than women and although occasionally seen in children it is more likely to occur in adolescence and earlier adult life being uncommon after 50 years of age It is usually due to chronic suppuration especially in bone chronic tuberculosis and syphilis It rarely occurs in other chronic infections but it has been described in severe rheumatic heart disease and a certain amount of amyloid change has sometimes been found post mortem in patients suffering from chronic cardio vascular disease and chronic nephritis in the absence of chronic suppuration As it is a degenerative change it has however more affinity with nephrosis than with nephritis

Pathology —Amyloid material or lardacein is a product of protein degeneration and consists of protein linked with chondroitin sulphuric acid The latter substance is a normal constituent of elastic tissue and cartilage In uncomplicated cases the affected kidney has the appearance of a large white kidney with a smooth surface and a capsule that strips easily The organ is firmer than it otherwise would be

On section the cortex is thicker than normal and has a yellowish white appearance the glomeruli may be visible as minute translucent spots The pyramids are dark red in contrast to the pale cortex If a solution of iodine in potassium iodide is poured over the surface, some of the glomeruli stand out as mahogany brown spots and the vasa recta as brown streaks In histological preparations stained with methyl violet amyloid material takes a pink colour The disease tends to appear first in the capillaries of some glomeruli while others are normal and its incidence is often partial within a single glomerulus The afferent arterioles vasa recta and capillary plexus are next affected, in more advanced cases there is amyloid degeneration of the tunica propria of the tubules with amyloid deposits in the interstitial tissue In most cases there is an associated nephritis The kidney lesion is generally the most striking part of a widespread lardaceous degeneration which also involves the liver spleen and intestine less commonly the blood vessels of the thyroid suprarenals pancreas, heart and brain may be affected as well Occasionally only the kidney is implicated

Symptoms —The onset is insidious and the symptoms are not likely to occur unless chronic suppuration has existed for at least 3 months

The urine is copious of low specific gravity (1 003 to 1 010) The amount of albumin is variable when abundant hypoproteinæmia may result. The amount of urine and its specific gravity may also be affected by the presence and degree of coincident nephritis and the state of the heart Hyaline and granular casts are present in the urine casts staining brown with iodine are not evidence of amyloid disease and may occur in other diseases of the kidneys True waxy casts are not found In later stages there is œdema with diminished excretion of urine The blood pressure is not raised, nor is the left ventricle hypertrophied unless there is coexistent chronic nephritis

Diagnosis —The condition must be distinguished chiefly from Type 2 nephritis The diagnosis of amyloid disease is made (1) when there is a sufficient cause in the past history or present condition namely chronic suppuration or syphilis, (2) on signs of lardaceous disease in other organs such as enlargement of the liver or spleen and diarrhœa (3) on confirmatory evidence from special tests The Congo Red test is based on absorption of the dye by amyloid material and its consequent removal from the blood stream and failure to appear in the urine after intravenous injection of a known quantity of dye The test is positive in 80 to 90 per cent of cases When it is essential to be certain of the diagnosis (*e g* when a decision on surgical treatment of the primary infection must be made) drill biopsy of the liver will afford histological proof

Course and Prognosis —This depends on that of the primary cause If the latter is unchecked the disease is slowly progressive and death occurs from exhaustion due to the original disease or from uræmia Where the original disease can be cured recovery may occur Complete recovery of the kidneys is less likely than is recovery of the liver spleen and intestines This is probably due to associated nephritis

Treatment —The treatment is that of the original disease In suppuration of the bones or joints empyema etc it is surgical but it must be recognised that in advanced cases surgical treatment may be too late even though it is successful in eradicating the septic focus In all cases fresh air and sunlight and a nourishing diet are essential Iron and cod liver oil should be given Cases of syphilitic origin should be treated with appropriate antisyphilitic therapy

PYELITIS

Definition —Pyelitis is inflammation of the renal pelvis When complicated by nephritis the condition is termed pyelonephritis

Ætiology—Most cases are due to a blood borne infection of the renal pelvis The pelvis may also be involved by ascending infections—(*a*) via the lumen of the ureter when there is ureteral obstruction it is probable that infection does not spread by this channel when the lumen is normally patent (*b*) By way of the peri ureteral lymphatics from local foci in lower parts of the urinary tract such as the bladder urethra prostate seminal vesicles and epididymis Lastly there is the possibility of direct spread of infection from the bowel and by cross lymphatic channels from one kidney to the other In those cases in which a pyelitis occurs secondary to appendicitis cholecystitis ulcerative colitis etc the spread of infection may be by the lymphatics or the blood stream

Pyelitis is more common in females than in males Its age incidence depends on the determining cause Thus it is common in female infants as a result perhaps of urethral infection to which they are more liable than male infants It is not an uncommon complication of pregnancy occurring especially in the fifth month of gestation It is common in males at a later age associated with enlarged prostate and cystitis

In general terms any injury or disease of the renal pelvis or any condition which interferes with the normal flow of urine may be the determining cause of pyelitis Thus it is a common complication of hydronephrosis from whatever cause It often complicates stone in a kidney, tuberculosis of the kidney and new growths of the renal pelvis

Pathology—The mucous membrane of the pelvis is swollen œdematous and hyperæmic and the submucous venules are engorged Where there is obstruction the pelvis is dilated and contains a slightly turbid or opalescent fluid In these circumstances the ureter above the obstruction is dilated and tortuous and its walls are thickened The kidney is swollen and pale, from cloudy swelling and in severe cases there may be multiple small abscesses in the renal parenchyma

Bact coli is by far the most common infecting micro organism Streptococci staphylococci gonococci and bacilli of the *Proteus* and typhoid groups may be found The infecting micro organism is readily recovered from the urine

Symptoms—The clinical types of pyelitis differ greatly from one another, and the condition may be responsible for an acute fulminating illness or for chronic malaise of indefinite nature

Local Symptoms—Pain is the most important especially as a diagnostic indication in acute cases It is a dull ache in the loin or flank at first slight and intermittent later or in other cases at once constant and sometimes intense Occasionally it takes the form of renal colic At its onset the pain may be diffuse and abdominal Increased frequency and urgency of micturition is the most common symptom There may be strangury

General Symptoms—In acute cases there may be sudden onset with rigors vomiting headache and the general constitutional disturbance of profound toxæmia These cases may simulate septicæmia (in fact there may be septicæmia) appendicitis or when associated with abdominal distension constipation and vomiting may even simulate intestinal obstruction In other cases with cerebral symptoms meningitis may at first be difficult to exclude

In subacute cases without marked pain or rigors there is general malaise fever anorexia wasting and a secondary anæmia associated with some degree of polymorphonuclear leucocytosis (white blood count=10 to 15 000)

In relapsing cases there are periods of exacerbation with acute symptoms and intervening periods of fair health or general malaise Fever is commonly present in acute cases with rigors it may rise to 105 or 106 F In general the temperature is irregular remittent or intermittent varying between 102 and 104 F in acute cases and 100 and 102 F in subacute cases The pulse is raised in proportion to the temperature and there is a corresponding slight increase in the respiration rate

Of other general symptoms constipation or diarrhœa frequently precedes the disease and constipation generally accompanies it Toxæmia is often marked

Deep tenderness on palpation of the renal region and the presence of infected urine are the diagnostic signs of the disease There is some degree of abdominal rigidity, and it may be possible to determine enlargement and tenderness of the kidney The urine is passed in small quantities at frequent intervals It has the usual characters of febrile urine and is turbid The turbidity or an opalescence is still present after filtration When an appreciable quantity of pus is present it settles at the bottom of a specimen glass in a thick whitish deposit Examination of the deposit (catheter specimen in women) shows pus cells and epithelial cells from the urinary tract There may be hæmaturia

Bacteriuria—In this condition bacteria are present in the urine in such quantity as to make it hazy to the naked eye but there is little or no inflammatory reaction in any part of the urinary tract Hence there are no localising symptoms and few pus cells The urine when freshly passed has a hazy appearance In a test tube, when the tube is rotated, the urine has a "satiny" appearance or shimmer It is not cleared by filtration It often has a fishy smell in *Bact coli* infection, and is ammoniacal in smell in *Proteus* infection Its reaction is acid unless due to staphylococcal or *Proteus* infection It generally contains a trace of albumin and often may contain a few white blood corpuscles and epithelial cells A catheter specimen grown in broth in dilutions of 1 ml, $\frac{1}{10}$ ml and $\frac{1}{100}$ ml urine in 10 ml broth gives a growth in all dilutions and in *Bact coli* infections there is generally a growth in greater dilutions Streptococcal and staphylococcal infections are less common but even when present they are easily overlooked because the streptococci and some forms of staphylococci are liable to be overgrown by the *Bact coli* on culture Thus an infection by *Streptococcus fæcalis* may be first recognised only after the *Bact coli* infection has been eradicated by treatment

Diagnosis—When there is fever and constitutional disturbance without localising signs or symptoms the differential diagnosis is from those diseases which come in their early phases under the category of indeterminate fever The diagnosis is established by examination of the urine Pyonephrosis is diagnosed by the presence of a renal swelling Calculus is recognised by its clinical features and by radiography Perinephric abscess in its early stages is not accompanied by pyuria or increased frequency of micturition Cystitis is generally afebrile and it is accompanied by suprapubic discomfort and pain, particularly at the end of micturition, the diagnosis can be established by cystoscopy Urethritis is recognised by local tenderness urethral discharge and the appearances on urethroscopy and prostatitis by swelling and tenderness on rectal examination

Prognosis—The usual outcome of uncomplicated pyelitis with efficient treatment is recovery in 5 to 10 days Efficient treatment depends on the use of the drug namely a sulphonamide or penicillin to which the infecting micro organisms are sensitive When these remedies fail streptomycin may be effective within 24 or 48 hours even in the presence of a complication such as one or more stones in the kidney These new remedies have greatly diminished the risk of ascending suppurative nephritis pyonephrosis or chronic pyelonephritis

Treatment—Prophylaxis is important in nurseries and children s hospitals since there is evidence of spread of infection via the urethra in females Here it is a question of cleanliness In general terms exposure to cold over fatigue and loose stools are to be avoided when there is susceptibility to *Bact coli* infection of the urinary tract

A patient suffering from an acute attack is treated with rest in bed, fluids in large quantity, bowel function is regulated and sufficient alkali is given by mouth to make the urine alkaline In order to avoid chill the patient is nursed between blankets Five to 6 pints of fluid are given in every 24 hours in the form of water

barley water imperial drink weak tea and thin soups Milk may be citrated and as the temperature subsides diet is increased by the addition of starch fruit and vegetables Bowels are emptied with an initial laxative followed by an enema if necessary After this the action of the bowels is regulated with paraffin magnesia or mild laxatives such as liquorice powder rhubarb or aloes It is important to avoid habitual loose stools because this predisposes to urinary infection A mixture containing 30 g each of potassium citrate and sodium bicarbonate is given 3 hourly until the urine is alkaline Every specimen of urine passed is tested with litmus paper When the urine is alkaline the mixture is given at 4 or 6 hourly intervals that is to say in sufficient quantity to keep every specimen of urine alkaline

The alkali treatment of *Bact coli* infections of the urinary tract is now only given in the initial stage of the more acute cases and even in these with increasing experience of the efficacy of sulphonamide drugs in the treatment of urinary infections one of these drugs is given as soon as the disease is diagnosed Sulphacetamide is the drug of choice for *Bact coli* infections because of its low renal toxicity It is readily absorbed rapidly eliminated and is very soluble (much more so than sulphadiazine) Hence a high urinary concentration can be obtained with a relatively low blood level In an acute case with high fever and a large fluid intake 1 g is given 4 hourly As soon as the temperature subsides and the fluid balance in the patient is restored to normal the dose of sulphacetamide is reduced to one tablet 4 hourly and at the same time the fluid intake is limited to 2 pints in 24 hours This treatment is given until the urine is perfectly clear when freshly passed it is then continued for a further 48 hours In a mild or chronic case the length of treatment is generally 5 to 6 days In an acute case it may be considerably longer Forty eight hours after the drug is stopped the urine is again examined bacteriologically If the urine is still infected the diagnosis should be reconsidered

In the first place the infection may be a complication of concealed disease of the urinary tract such as calculous disease tuberculosis neoplasm enlarged prostate with residual urine or hydronephrosis Chronic pyelonephritis especially if of long standing may resist sulphonamide therapy Rarely a persistent infection may be a complication of organic disease of the digestive tract such as chronic appendicitis especially if the right ureter is involved diverticulosis or even cholecystitis In any case of urinary infection that is resistant to treatment or presents any unusual symptom a detailed investigation of both urinary and digestive tracts is required in order to determine or exclude a change in structure which may be the underlying and determining cause of the urinary infection

In the second place when the *Bact coli* infection has been cleared by sulphonamide treatment a residual infection with *Str fæcalis* or staphylococcus may be found It is important to clear the urine of these residual infections because they may determine a return of *Bact coli* infection Mandelix may be used for *Str fæcalis* infection The routine is to give ammonium or calcium mandelate gr 45 in solution (2 g) with 2 oz of water four times in 24 hours Fluid intake is limited to 32 oz which together with the medicine makes a total intake of 2 pints Every specimen of urine passed is examined as to its *p*H which must be 5 to 5 1 and sufficient ammonium chloride is administered by mouth to produce the required urinary *p*H

Penicillin given intramuscularly is almost wholly excreted in the urine where a high concentration is therefore attained Penicillin is now used for staphylococcal *Str fæcalis* and *Proteus* infections of the urinary tract as also in the unusual cases in which the *Bact coli* is penicillin sensitive Penicillin has therefore displaced sulphathiazole in the treatment of staphylococcal infections and mandelic acid in the treatment of *Str fæcalis* infections An average dose is 20 000 units 6 hourly throughout the 24 hours It is probable that the most effective treatment for Gram negative bacillary infections of the urine will prove to be streptomycin given intramuscularly

4 hourly in a dose of 0 5 g, namely 3 g daily for 2 days With further experience smaller doses may be found effective and 2 days treatment may prove sufficient.

In the uncommon fulminating cases with unilateral suppurative nephritis, nephrectomy may save the patient s life

CHRONIC PYELONEPHRITIS

It has already been stated that infection may spread from the renal pelvis into the kidney substance and produce pyelonephritis The recognition of this extension is difficult in the early stages because renal involvement is focal so that the diagnostic signs of nephritis are absent In severe cases of pyelitis however, a slight degree of œdema and hypertension may be observed A further pointer to the diagnosis is the persistence of albuminuria when the pyelitis has been effectively treated and pus and organisms are no longer found in the urine In chronic pyelitis, particularly when there are recurrent attacks over a period of years, the presence of chronic pyelonephritis is strongly presumptive An acute ascending infection particularly when drainage is defective, as in neurogenic retention of urine, may lead to suppurative pyelonephritis with the formation of multiple small abscesses Fever and toxæmia are severe and in such cases pyuria may persist in spite of antibiotic therapy A particularly intense and often fatal type of suppurative pyelonephritis occurs in diabetes and especially in elderly patients extensive medullary necrosis may be produced (see p 1127)

The particular importance of chronic pyelonephritis lies in the fact that it may persist and progress after the pelvic inflammation has subsided Gradual destruction of the renal parenchyma continues over a period of many years, usually in the absence of symptoms and the clinical course resembles very closely that of chronic Type 1 nephritis The similarity is further enhanced by the observation that a large proportion of patients presenting with this condition in its late stages give no history of acute pyelitis The incidence of this form of the disease is much higher in women than in men which suggests that sub clinical pyelitis may possibly have occurred during pregnancy at some time in the past

Pathology—Pyelonephritis is an interstitial inflammation of the kidney which leads to focal scarring and destruction of nephrons extending upwards from the medulla to the cortex Involvement of the kidney may be irregular, so that scarring may be confined to a single area, or may involve broad zones throughout the substance of the kidney This leads to the characteristic rat bitten appearance of the outer surface which is deformed by broad sunken scars While both kidneys may be involved to a similar extent, pyelonephritis is usually more marked in one kidney than in the other and there may be gross inequality in size Not infrequently one kidney alone is involved, the other showing compensatory hypertrophy It is highly probable that local obstructive lesions such as have been discussed under acute pyelitis are responsible for this uneven distribution Obstruction is also indicated by the presence of some degree of hydronephrosis although this may be slight Microscopically there is in many cases little evidence of active pyelitis but some degree of sub pelvic fibrosis is usually seen In the renal substance areas of scarring with dense round cell infiltration alternate with normal kidney tissue In the fibrotic zones the tubules are atrophied and characteristically groups of surviving tubules are seen in the cortex distended with hyaline material and presenting an appearance resembling thyroid tissue The glomeruli in the affected zones show ischæmic atrophy with hyaline thickening of Bowman s capsule aggregates of completely hyalinised glomeruli in the shrunken areas of the cortex are typical Occasionally glomeruli in the less affected areas show great dilatation and wavy distortion of Bowman s capsule the capsular space being filled with albuminous material In severely scarred kidneys

medium and large arteries are often prominent and show obliterative endarteritis Arteriolar changes are inconspicuous except in those rare cases which are complicated by malignant hypertension

Symptoms—There may be no symptoms in chronic pyelonephritis until attention is drawn to the condition by the development of uræmia or hypertension Alternatively there may be recurrent attacks of pyelitis or cystitis High blood pressure is not a common or prominent feature of chronic pyelonephritis nevertheless in some cases severe hypertension is observed and may progress to the malignant phase This complication is occasionally seen in unilateral disease It is difficult to say why only a minority of patients with pyelonephritis develop hypertension but there is a possibility that some other factor such as a congenital obstructive lesion of the kidney or even a constitutional tendency to hypertension may be responsible Albuminuria is usually present throughout the course of pyelonephritis the urine may also contain pus and bacteria but in many cases the ascending infection has resolved and pyuria is absent occasionally the urine may even be free from albumin A diagnosis of essential hypertension is then likely to be made and the underlying condition is only revealed when intravenous pyelography shows distortion of the renal calyces or evidence of renal contraction In the absence of hypertension uræmia may be so protracted in chronic pyelonephritis that osteodystrophy with metastatic calcification occurs In very rare cases chronic acidosis leads to severe sodium depletion and hypotension (so called salt losing nephritis) so that the clinical picture may closely resemble Addison s disease

Diagnosis—Persistent albuminuria associated with renal impairment with a past history of attacks of pyelitis will suggest the diagnosis Many patients with other forms of Bright s disease develop urinary tract infection however so that there will often be an element of doubt In the late stages the presence of uræmia with little or no hypertension should bring to mind the possibility of chronic pyelonephritis Intravenous pyelography should not be carried out if there is impaired concentrating power since concentration of the radio opaque solution is also defective Retrograde pyelography may show distortion of the renal calyces but this investigation is hardly justified in the presence of renal insufficiency

Prognosis—This depends on the extent of the lesion *i e* whether it is unilateral or bilateral and on the effectiveness with which active urinary tract infection can be controlled In established bilateral disease progress is very slow largely due to the absence of severe hypertension and the patient may continue in good health for 10 or 20 years before uræmia develops Even the stage of renal insufficiency tends to be protracted and consequently a long period of ill health must be expected in the later stages of the disease

Treatment—Active infection of the urinary tract should be treated as described under pyelitis Nephrectomy should be considered in unilateral pyelonephritis and particularly if hypertension is present Many cases have been reported where nephrectomy has been a life saving measure after the hypertension had entered the malignant phase *i e* when *papillœdema had developed* When renal failure develops treatment is that described for the corresponding stage of chronic Type 1 nephritis

PERINEPHRITIS AND PERINEPHRIC ABSCESS

Suppurative perinephritis may be due to blood stream infection when the invading organism is usually *Staphylococcus pyogenes* or it may arise from direct extension of local suppuration the invading organism being a member of the coliform group or other bowel pathogen

Ætiology and Pathology—Blood stream infection may follow injury, but more

frequently results from boils carbuncles and tonsillitis or complicates an acute specific fever J Koch has shown experimentally that intravenous injection of staphylococci is followed by their excretion in the urine after an interval of 4 to 6 hours In the process of excretion, according to Koch they may give rise to multiple cortical abscesses, cylindrical medullary abscesses, or, passing along the cortical lymphatics may gain access to the perinephric tissues and there cause abscess formation In these circumstances perinephric abscess is an example of staphylococcal pyæmia with single metastatic abscess formation Perinephritis by direct extension may complicate suppuration in the neighbouring organs, such as the kidney liver gall bladder or appendix It may be secondary to caries of the spine In other cases the infection may be carried by lymphatics from a focus in or around the bladder, rectum or female pelvic organs

Symptoms —The onset is generally gradual It is characterised by fever and malaise as in typhoid fever There may be no local symptoms for the first 7 to 14 days and during this period there is increasing toxæmia general abdominal discomfort or pain slight fullness and resistance, with deep tenderness in the affected loin As the abscess forms, pain and tenderness increase, there is induration and later, redness of the skin and œdema in the lumbar region The tumour first tends to spread backwards, obliterating the normal hollow in the loin and then as pus collects it may spread forwards forming a tender tumour palpable from the front In its relations to the colon it resembles a renal tumour, but does not move with respiration There is resistance or rigidity of the abdominal wall on the affected side There is an increasing polymorphonuclear leucocytosis up to 20 000 or even 40 000 *The urine is febrile in character, containing a trace of albumin and perhaps* a few white blood corpuscles, it does not contain pus, unless the kidney itself is involved, but hæmaturia may occur In some cases the disease runs an acute course and there may be rigors at an early stage

Diagnosis —Before localising signs appear the disease may be mistaken for typhoid fever, malaria or septic endocarditis The blood examination is important for the purpose of excluding malarial parasites leucocytosis is against typhoid fever and when above 15,000 is in general against infective endocarditis Absence of agglutination of micro organisms of the typhoid group is further evidence

When the tumour exists it has to be distinguished from a renal tumour or pyonephrosis Renal and adrenal growths may be accompanied by fever but do not usually give the general symptoms of suppuration they tend to extend forwards rather than backwards and induration of the tissues is absent Pyonephrosis causes symptoms of suppuration and a tender swelling but the tumour is circumscribed moves with respiration and does not cause any bulging in the lumbar region Pyuria is usually present

The diagnosis from caries of the spine, hip disease and even of myositis as distinct from perinephritis may be difficult Since perinephritis in itself induces lumbar rigidity and some degree of scoliosis radiographic examination may be required to exclude caries of the spine This investigation is also important since a diagnostic radiological sign of perinephric abscess is obliteration of the psoas shadow on the affected side Hip joint disease is excluded by absence of local tenderness and by the freedom of flexion and rotation of the thigh

Course —When the condition is simply associated with chronic nephritis it has no separate significance When it proceeds to suppuration the abscess may rupture into the peritoneum, colon or pleura, or on to the surface, unless the abscess is opened and drained

Treatment —The patient is treated at rest in bed and given penicillin—30 000 units 4-hourly Alternatively, sulphathiazole is prescribed namely an initial dose of 2 g followed by 1 g 4 hourly Fomentations or a kaolin poultice are applied to the loin Aspirin is given to relieve pain *If there is evidence of abscess formation*

an operation is performed and the pus evacuated penicillin being instilled into the abscess cavity

TUBERCULOSIS OF THE KIDNEY

Small grey tubercles are frequently found scattered through the kidneys in persons who die of acute miliary tuberculosis the kidney disease however scarcely affects the clinical aspect of the case and this form of renal tuberculosis will not be considered here Further in patients who die of pulmonary tuberculosis it is not uncommon to find tuberculous foci in the kidneys post mortem although there was no indication of their presence during life

Clinical renal tuberculosis is either the fibro caseating form of the disease or it is tuberculous hydronephrosis In either case the tuberculous infection is generally primary in the kidney in so far as its clinical expression is concerned

Ætiology—It is more common in women than men The maximum age incidence is in the third and fourth decades the disease is uncommon in the young and rare in the old At an early stage the disease is unilateral In the majority of cases the tubercle bacilli are carried to the kidney by the blood stream from a tuberculous focus such as a caseating lymph gland Recent experimental work has shown that bacteria do not ascend in the lumen of the ureter unless it is diseased when the infection may spread by direct extension in its walls Infection may also reach the kidney via the lymphatics in a proportion of cases The path of infection is by way of the ureteric lymphatics and it is probable that in pelvic tuberculosis for example tuberculous prostatitis may spread to the kidney by this route There is also reason to think that tubercle bacilli from a diseased kidney may infect the opposite healthy kidney by the same lymphatic path the bacilli first travelling in the urine and walls of the ureter from the diseased kidney and causing disease of the bladder and then travelling from the bladder by way of the ureteric lymphatics to the sound kidney On the other hand there is a shorter path for infection from one kidney to another by the para aortic lymphatic system Since the disease in the other kidney takes the same anatomical form as it originally had in the kidney first affected it is probable that, if the first is due to a blood borne infection so is the second Vesical tuberculosis is as a rule secondary to infection elsewhere in the urino genital system commonly in the kidneys

Pathology—The initial lesion is in the cortex or one of the pyramids and it consists of one or more tubercles The morbid process spreads by destruction of kidney tissue there is caseation in the centre of the lesion inflammatory reaction with intense small cell infiltration giant cell formation and more or less fibrosis at the periphery The lesion also spreads by the deposition of tubercles at a distance these are scattered through the cortex singly or in groups Extension through the capsule is uncommon but extension to the renal pelvis is frequent Complete destruction of one or more pyramids may occur or the disease may spread and involve one or more calyces or the entire pelvis The resulting infiltration and cicatricial contraction may lead to hydro or pyonephrosis The disease tends to extend down the ureter and the bladder is commonly infected at an early stage Secondary infections may lead to metastatic abscesses in the kidneys and ultimately to destruction of the whole organ

Symptoms—Frequency of micturition is often the earliest symptom it is first noticed by day and later at night Urgency and painful micturition develop next and are due to tuberculous cystitis The urine may show no other abnormality than a trace of albumin at an early stage characteristically it is pale and a little turbid from the presence of pus it is acid in reaction it may contain a few renal cells and it is sterile on culture By appropriate staining tubercle bacilli may be demonstrated

in the centrifugal deposit Hæmaturia may be the first symptom or the disease may develop insidiously with lumbar pain On examination the kidney is sometimes enlarged and it may be hard and irregular, it is often tender Tenderness along the course of the ureter or thickening of the ureter, as determined by abdominal or rectal examination, is of great importance The rest of the urino genital system requires close examination, this should include cystoscopy and in some cases ureteral catheterisation Radiographic examination of the abdomen may reveal calcified tuberculosis of the kidneys or lymph glands and it may be required in the differential diagnosis from renal calculus Finally, a careful review of the patient s history and present condition for evidence of a chronic bacterial toxæmia or of tuberculous infection elsewhere must be made

Diagnosis—The presence of tubercle bacilli in the urine whether determined by microscopic examination of the stained deposit or by guinea pig inoculation is not absolute proof of renal tuberculosis, because the bacilli may be excreted by a healthy kidney or they may come from some other part of the urinary tract Nevertheless the demonstration of tubercle bacilli in the urine is of the first importance in a doubtful case and the diagnosis may be established by cystoscopy The cases which require most careful examination are those with an atypical onset, such as massive hæmaturia, and those in which there is a gross secondary infection when first seen The possibility of renal tuberculosis must always be borne in mind in hydro and pyonephrosis The differential diagnosis from simple albuminuria and the several forms of Bright s disease is made on the presence of pyuria and the absence of signs and symptoms of chronic nephritis

Course and Prognosis—The onset is insidious and the course progressive Natural recovery is hardly known though occasionally an unsuspected caseous kidney may be found at autopsy in patients dying of other diseases The disease runs an uncertain course having a duration of a few years up to 10 or 12 years from the date of diagnosis Death results from tuberculous toxæmia, secondary infection or failure of renal function

Treatment—When the disease is unilateral the kidney should be removed but nephrectomy is rarely justified if the other kidney is involved In any case the patient s health and resistance should be raised to the utmost by rest fresh air and good food on the general lines of treatment of tuberculosis of the lungs Therapeutic trials of the specific remedies against tuberculosis, streptomycin with isoniazid or sodium amino salicylate, have shown that renal tuberculosis is more resistant to treatment than other forms of the infection and further experience is required before their effectiveness can be assessed

RENAL CALCULI (NEPHROLITHIASIS)

Renal calculi may be composed of calcium oxalate or phosphate, uric acid urates phosphates, cystine or of a mixture of these

Ætiology—All these materials are sparingly soluble in water and their solubility in urine is dependent on (i) its *p*H If this stands at 5 uric acid is precipitated while phosphates and carbonates are deposited at *p*H about 8, the others at some intermediate point (ii) On the presence of urea which renders both uric acid and oxalates more soluble (iii) The protective action of certain non albuminous colloids If these become coagulated their protective influence is lost Any condition which interferes with the free flow of urine and so leads to stagnation predisposes to and may determine the formation of calculi Thus prolonged recumbency as after fracture of the femur may determine calculus formation due to stagnation in the dorsal portion of the calyces Infection of the urinary tract may be secondary to the calculus but it is also a cause of calculus formation by altering the colloid content of the urine or

by its effect on the pH of the urine Metabolic disorders may be a factor in some cases as for instance in the uric acid stones which may occur in young children Hyperparathyroidism leads to excessive mobilisation of calcium from the bones and this is followed by ' metastatic calcification in various tissues including the kidneys Hot climates tend to favour stone formation owing to concentration of the urine due to excessive sweating

Pathology —The pure oxalate stone is very hard mulberry shaped stained by altered blood and varies in size from that of a mere granule to that of a walnut If it is encrusted with uric acid it becomes brown and in form a coral shaped mass representing a cast of the renal pelvis and calices Phosphatic stones are generally smooth and white A cystine stone is hard oval light amber or greenish in colour with a glistening surface Other forms are rare If the stone remains in the renal pelvis it may (1) by gradually increasing in size lead to the atrophy of the renal tissue (2) by eroding the capsule of the kidney produce a fistula into the perinephric tissues resulting in a perinephric abscess (3) by obstructing the outflow of urine cause hydronephrosis or more frequently pyonephrosis If it passes into the ureter it may become impacted in this way again exciting hydronephrosis or pyonephrosis or if it obstructs the ureter completely, may produce atrophy of the kidney If it causes ulceration of the ureter this may be followed by stenosis If it passes into the bladder it is very likely to excite ammoniacal decomposition and thus become encrusted with phosphates

Symptoms —A stone may remain latent in the kidney without causing any symptoms More usually it causes pain particularly on any jolting movement This is occasionally referred to the opposite side a point to be borne in mind when considering operation A bout of pain may be accompanied by hæmaturia and there may be albuminuria for some days afterwards A small oxalate stone may produce more pain than a large uratic stone because of its hardness and roughness A large branched uratic stone occasionally causes profuse hæmaturia without any pain The results of renal calculi may be classified as (*a*) mechanical (*b*) septic Under the first heading come colic hæmaturia anuria hydronephrosis under the second pyelitis perinephric abscess pyonephrosis

Renal colic is the most severe and distressing manifestation of calculus It is particularly likely to be started by riding on a horse or in a jolting vehicle which causes the calculus to engage in the entrance to the ureter Violent paroxysms of pain then occur radiating along the course of the genito crural nerve down into the groin and testis which becomes retracted in the scrotum The pain is also felt in the loin and the muscles overlying the kidney become rigid Vomiting and sweating are common The patient is unable to keep still and rolls about or gets on to his hands and knees calling out with each paroxysm He becomes pale and his pulse increases in frequency and the temperature is apt to rise During or after the attack there is usually some hæmaturia and crystals may be found in the urine The attack may last several hours and then end as abruptly as it began Anuria is a serious symptom and implies that the ureter is completely blocked and the other kidney is either diseased or its secretion reflexly inhibited Occasionally both ureters may be blocked by calculi Symptoms referred to the bladder prostate or seminal vesicles do not occur until the stone reaches the bladder or the lower end of the ureter

Diagnosis —The occurrence of renal colic and hæmaturia suggests stone but these symptoms may be produced by the passage of a blood clot from renal neoplasm or by acute pyelitis especially in a movable kidney Ordinary examination of the abdomen reveals nothing beyond lumbar tenderness in uncomplicated cases Radiographic examination is of great value Oxalate stones are the easiest to detect by this method as even when small they throw a dense shadow This is fortunate since oxalate stones are the commonest Pure uratic stones may not be detected unless they are large Cystine stones throw a less dense shadow than calcium oxalate stones

Calcareous abdominal glands and phleboliths may be mistaken for calculi on radiographic examination In doubtful cases, pyelography, intravenous or instrumental should be done A radiograph of the pelvis should never be omitted, since a stone may have passed down to this region Attacks of pain and hæmaturia with the presence of calcium oxalate crystals in the urine but with a negative radiographic examination are probably due to crises of oxaluria Appendicular colic may simulate renal colic, but the point of maximum tenderness is different

Prognosis —As long as there is no serious destruction of kidney substance or septic complication the outlook as to life is good, if treatment is adequate Attacks of renal colic may occur from time to time with great suffering and even after stones have been removed by operation they may form again Occasionally stones may be followed by chronic pyelonephritis with its usual consequences

Treatment —Indications for treatment are provided by the ætiological factors already discussed In any case of long recumbency the patient must lie on his face several times in the 24 hours Any condition of stasis in the urinary tract will be dealt with as far as is possible The treatment of infected urine is described under pyelitis If a renal calculus is present and this is confirmed by radiography removal by operation is indicated The following points however, are generally contraindications for operation (i) large bilateral stones, (ii) stones which are only the size of a pea or smaller, unless there is severe pain extensive absorption of renal substance causing toxic symptoms, or obstruction to the outflow of urine If a small stone is not passed as a result of medical treatment, its removal by operation should be seriously considered, (iii) in some patients small calculi are repeatedly formed and passed In these cases operation is better postponed because of the likelihood of recurrence If the diagnosis is uncertain or operation is refused or postponed or considered inadvisable because of the patient's general condition the treatment appropriate to the deposit found in the urine should be continued Violent exercise and jolting movements should be avoided Small stones can often be got rid of by giving the patient 5 to 10 minims of tincture of belladonna with gr 10 of potassium citrate every 4 hours for a few days, and directing that 5 pints of water should be taken in the 24 hours For the symptomatic relief of pain aspirin in 10 grain doses hot baths and kaolin poultice (antiphlogistine) may be of service Morphine should be avoided in the treatment of chronic renal pain on account of the danger of establishing a habit

For an attack of renal colic morphine gr $\frac{1}{6}$–$\frac{1}{4}$ together with atropine sulphate gr $\frac{1}{100}$ should be given hypodermically The anti spasmodic effect of the atropine aids the onward passage of the stone while the morphine relieves the pain If morphine be given alone, the pain is apt to recur as soon as its anodyne effect passes off Ten minims of tincture of belladonna should then be given in an ounce of water every 3 or 4 hours with abundant fluids, as described above until the pupils are dilated and the face rather flushed Hot applications to the loins or hot baths may help to relax spasm After the paroxysm is over a radiograph should be taken to locate the stone if it has not been passed

HYDRONEPHROSIS

Definition —A condition in which the pelvis and calyces of the kidney are distended by the accumulation of non infected urine due to ureteral or urethral obstruction

Ætiology —CONGENITAL —The condition may be congenital due to an abnormality of the ureter or urethra other congenital defects may be present The ureteral stricture is commonly found at the exit of the ureter from the pelvis of the kidney or near its entrance into the bladder Congenital narrowing of the ureter is much

more common than was previously recognised Other congenital causes are a faulty connection of the ureter to the pelvis of the kidney or an aberrant renal artery Hydro nephrosis is sometimes found post mortem in infants and children without evidence of obstruction to the outflow of urine In these cases the condition is presumed to be due to a neuro muscular inco ordination comparable to congenital hypertrophic stenosis of the pylorus

ACQUIRED —It is more common in females than in males and the maximum age incidence in 74 cases collected by Herringham was between the third and sixth decade

(*a*) *Bilateral* hydronephrosis results from stricture of the urethra phimosis enlarged prostate obstruction within the bladder or from a pelvic tumour the last named is the commonest cause

(*b*) *Unilateral* hydronephrosis is due to ureteral obstruction from—

1 Obstruction of the lumen by a stone growth or blood clot
2 Stricture of the ureter following ureteritis
3 Pressure from without due to growths
4 Torsion of the ureter by displacement of a movable kidney It is also thought that chronic prostatitis or cervicitis may cause sufficient inflammation to produce some dilatation of the kidney pelvis and upper ureter which lengthens and thus kinks the latter

Pathology —Two types of hydronephrosis are recognised namely the pelvic type due to upper urinary tract obstruction and the renal type from obstruction to the lower tract In the former the pelvis of the kidney is dilated and there is less absorption of renal parenchyma in the calyces In the latter the calyces are more dilated and there is considerable destruction of kidney substance

It is generally held that hydronephrosis results from intermittent obstruction It has been produced experimentally however by ligature of the ureter causing complete obstruction But complete obstruction is more usually followed by atrophy of the kidney

Symptoms —Many cases are latent and give rise to no symptoms The tumour may be discovered accidentally or there may be complaint of pain in the flank or back The onset is insidious

The symptoms by which a hydronephrosis is indicated are the presence of a renal tumour and complaint of an aching pain in the flank or back and sometimes polyuria or hæmaturia In intermittent hydronephrosis the tumour suddenly disappears with the passage of a large quantity of watery fluid after an interval the tumour gradually reappears and finally empties suddenly as before This sequence may be repeated at intervals Where true polyuria or hæmaturia occurs it is due to a coincident nephritis or pyelitis There may be acute exacerbations of the chronic pain with vomiting and collapse such attacks may accompany emptying of the hydronephrotic sac

Diagnosis —The condition especially when bilateral and unaccompanied by symptoms is generally overlooked In its most characteristic form where the hydro nephrosis is intermittent the diagnosis is readily made When the condition is apparent simply as a renal tumour the diagnosis from renal neoplasm (or retro peritoneal glands in a child) is difficult When the tumour is large it may be mistaken for an ovarian tumour A urinary infection is often the first sign of hydronephrosis The diagnosis can be established by intravenous pyelography supplemented if neces sary by instrumental pyelography Aspiration of the sac has occasionally been done for diagnostic purposes but surgical exploration is a safer measure Fluid from a hydronephrotic kidney is clear or slightly turbid it contains albumin and traces of urea and other urinary constituents in the deposits there are epithelial cells

Course —When unilateral hydronephrosis may never cause serious trouble and intermittent cases may persist for years In bilateral cases uræmia may supervene

Infection of the kidney is not uncommon, and may lead to acute pyonephrosis The sac may discharge spontaneously through the ureter, and the fluid never reaccumulate The sac may rupture into the peritoneum or rarely through the diaphragm into the lung Cases have occurred in which the ureter of the sound kidney has been blocked by a calculus

Prognosis—This depends on the cause of the hydronephrosis and the condition of the opposite kidney

Treatment—The first indication is to remove the cause A narrowing of the ureter, generally congenital, or stenosis at the ureteropelvic junction are especially important causes of hydronephrosis Whereas in the past slight cases of hydronephrosis were treated on general lines and nephrectomy was performed for large hydronephrotic kidneys nowadays slight cases of hydronephrosis are examined with the greatest care and surgical treatment is more often undertaken as a preventive measure An abdominal belt or nephropexy may prevent the development of hydronephrosis in a movable kidney When a hydronephrotic kidney is infected the infection should be eradicated and with modern methods of treatment (see treatment of pyelitis) this can sometimes be achieved

In unilateral hydronephrosis causing serious symptoms or of large size, a plastic operation or nephrectomy is advisable Since the state and function of the opposite kidney can be fairly accurately ascertained by pyelography and examination of a sample of urine obtained by ureteral catheterisation nephrectomy is a less serious risk than it was before these exact methods of diagnosis were available

In bilateral hydronephrosis the main indication is to remove the cause when possible and to adopt every measure that may aid in preventing infection of the urinary tract

PYONEPHROSIS

Definition—Distension of the renal pelvis with pus to an extent sufficient to cause a renal tumour

Ætiology—The affection is a sequela of pyelitis or hydronephrosis There are two main types namely tuberculous and pyogenic pyonephrosis The latter which is the commoner, is most frequently due to an impacted calculus

Symptoms—The patient is wasted toxic and febrile Rigors are common There is a renal tumour which is tender on palpation and moves to some extent with respiration Pyuria is present unless the ureter is completely obstructed

Diagnosis—The differential diagnosis from hydronephrosis is made from the presence of pyuria and of local and general symptoms of bacterial infection Perinephric abscess gives signs of a more diffuse swelling usually with œdema and redness of the surrounding skin and does not move with respiration

Treatment—In bilateral cases the treatment is palliative In unilateral cases nephrectomy is indicated if tests show that the other kidney is adequate

TUMOURS OF THE KIDNEY

BENIGN GROWTHS

These are of relatively slight importance

ADENOMATA are the most common occurring in the cortex or under the capsule They may be single or multiple multiple nodules commonly occur in sclerotic kidneys in old age They seldom attain any size

FIBROMATA are not uncommon as nodules sometimes multiple in the cortex or medulla LIPOMATA and ANGIOMATA are rare

MALIGNANT TUMOURS

DYSEMBRYOMATA —These tumours are found most commonly in children under 3 years and almost always under the age of 11 They are more often bilateral than carcinoma They consist of cells remaining at the embryonic level and failing to differentiate in any direction (Round celled Sarcoma) There is a stroma of undifferentiated fœtal connective tissue which resembles spindle celled sarcoma In some tumours some degree of differentiation may take place Thus these tumours may contain embryonic striped muscle primitive cartilage or nervous tissue and primitive poorly formed tubules can usually be found They are yellow and homo geneous on section

ADENOCARCINOMA OF RENAL TUBULES —The Grawitz tumour or hypernephroma is now recognised as an adenocarcinoma arising in tubular epithelium These tumours are single large well circumscribed and often surrounded by a capsule of compressed kidney tissue which is destroyed by pressure rather than by infiltration These tumours consist of solid anastomosing columns of cells Their blood supply consists of irregularly shaped lake like sinusoids which lie between the tubules of the growth in contradistinction to adenomata, which are composed of well formed tubules having well defined lumina and a simple capillary circulation Both in adenomata and adeno-carcinomata and especially in the latter the cells are infiltrated with a lipoid fat-glycogen complex (lipoid infiltration) which gives these tumours their peculiar yellow colour Recent and old hæmorrhage is commonly seen Cystic degeneration often occurs On section there is fine and coarse lobulation These tumours may spread along the renal veins into the inferior vena cava and to the pelvis of the kidney and perinephric tissues

Symptoms —1 Hæmaturia is the first symptom in more than 70 per cent of the cases It is much less frequent in children The blood is fluid or clotted and moulds of the pelvis or ureter may be passed The hæmaturia is spontaneous profuse and intermittent it is little influenced by rest nor is it provoked by exertion It may be the only evidence of a neoplasm and after lasting for a week or 14 days may cease leaving no further evidence of the growth until at some later date a tumour is felt The urine frequently contains albumin at intervals

2 Pain is uncertain It may be a dragging feeling or a constant ache The passage of clots may give rise to renal colic otherwise the hæmaturia is not accom panied by pain

3 The presence of a tumour is a most important sign It is felt on deep palpation bimanually It is first palpable below the ribs outside the rectus muscle as a solid swelling with rounded borders that moves with respiration It may be possible to define its upper border As the tumour increases it tends to go forward It may fill the hollow below the twelfth rib behind but does not cause a swelling in the back Large renal tumours cause asymmetry and bulging of the abdominal wall and marked displacement of neighbouring abdominal viscera On the right side the ascending colon lies in front on the left the last part of the transverse colon and the upper part of the descending colon the tumour is therefore resonant on percussion in front When the tumour is highly vascular pulsation is felt in it and a systolic bruit may be heard over it In later stages it is liable to become fixed by adhesions

4 Progressive emaciation is generally late It may be absent although the tumour is large

5 Metastases are sometimes the first sign of a renal neoplasm occurring in the lungs bones or brain Secondary deposits in the para aortic lymph glands may cause obstruction to the inferior vena cava or this may result from pressure of the tumour itself

Diagnosis —Diagnosis is made on the presence of hæmaturia with a tumour When hæmaturia occurs alone and other causes have been excluded by careful clinical

bacteriological and radiographic examination then a more detailed investigation of the urinary tract must be undertaken immediately This entails cystoscopy intravenous pyelography and on occasion retrograde pyelography When a tumour is the only sign an exploratory laparotomy is advised The tumour requires to be distinguished from splenomegaly, hepatomegaly and Riedel s lobe A renal tumour has not the definite edge characteristic of splenomegaly and enlargement of the liver Enlargement of the liver is not often a source of difficulty A Riedel s lobe is continuous with the liver, does not extend back into the loin and is dull on percussion Splenic tumours are recognised by the fact that they tend to occupy an oblique position in the abdomen by the presence of a notch and of a sharp inner margin, free movement with respiration and dullness to percussion

A differential diagnosis from retroperitoneal tumours including those of the suprarenal is not always possible though the suprarenal growths may sometimes be recognised by certain characteristic features Thus, there is the medullary sarcoma type described by Hutchison generally occurring in children characterised by metastases in the skull ecchymotic swelling of the eyelids papilloedema and severe anæmia, and the "infant Hercules" type of tumour of the adrenal cortex (see p 523)

Prognosis —The disease is almost invariably fatal Many die within 2 years, and the majority within 4 years, though exceptional cases of survival for 5 to 10 years after operation have been recorded

Treatment —*Surgical treatment alone holds out a prospect of cure* Symptomatic treatment includes the use of drugs for the relief of pain and the control of hæmaturia

CYSTS OF THE KIDNEY

SOLITARY CYSTS

These may occur in an otherwise normal organ They vary in size from very small cysts to tumours of considerable bulk They result from dilatation of an obstructed tubule and they may be congenital

MULTIPLE CYSTS

Multiple cysts of small size are commonly met with in sclerotic kidneys They result from chronic inflammatory changes that lead to obstruction of the tubules with subsequent dilatation There are also rare cases of multiple cysts of large size whose ætiology and course are little known

POLYCYSTIC DISEASE OF THE KIDNEYS

Definition —Polycystic kidneys appear as a massive conglomeration of cysts varying in size from a pin s head to a marble separated by dense strands of fibrous tissue in which little or no renal tissue is evident on naked eye examination

Ætiology and Pathology —The commonest age incidence is between 40 and 50 years they are relatively common in the decades preceding and following they may occur in infancy and childhood and of these a large proportion are in still born infants Those occurring in infants are congenital and other congenital abnormalities may be present The disease in adults is probably also congenital in origin In this case it must be progressive because the renal damage in the later stages is too severe to have been compatible with many years of active life In this connection it is noted that the disease is often found in more than one member of a family and in successive generations Its familial incidence congenital origin and association with cysts in

other organs especially the liver all suggest that this disease belongs to the group of congenital developmental errors

The organs are enlarged in size and weigh 20 to 30 oz each or even 3 to 4 lb They have been compared to a bunch of grapes in appearance The cysts project from the surface and form the mass of the organ They are lined by a layer of flat tened cells and are filled with fluid This fluid is clear or turbid limpid or viscid colourless or yellowish it is sometimes blood stained giving it a red purple or green colour Urea has been found in the fluid which may also contain fat globules cellular débris cholesterol and triple phosphate crystals On microscopic examination com pressed renal parenchyma is found in the septa between the cysts the tubules are distorted and exhibit varying degrees of atrophy degeneration and dilatation while the glomeruli show changes due to chronic ischæmic or hypertensive damage The blood vessels of the kidney undergo sclerotic changes there is increased fibrous connective tissue and small cell infiltration In some cases cysts are also found in the liver ovaries broad ligament uterus pancreas and spleen but they are rare in any other organ than the liver

Symptoms —The affection is nearly always bilateral When the tumours develop to large size in the fœtus difficulty in labour may result In the adult there may be no symptoms or any of the symptoms of chronic nephritis may develop and may terminate in uræmia cerebral hæmorrhage or cardiac failure General arterial disease with raised blood pressure and cardiac hypertrophy is commonly present on the other hand the condition may reach an advanced stage and fatal termination without appreciable cardiac hypertrophy In a third group the bilateral renal tumours are the most striking features associated with general malaise dull aching pain in the loins and recurrent hæmaturia The tumours are not tender and present the ordinary signs of renal tumours (*q v*) The urine is of low specific gravity and commonly contains a trace of albumin there may be polyuria

Diagnosis —The finding of albuminuria in association with large irregular bilateral renal enlargement should suggest polycystic disease Hydronephrosis pro duces a smooth rounded renal swelling Renal neoplasms other than sarcomata are nearly always unilateral The absence of fever and pyuria excludes bilateral pyo nephrosis Intravenous pyelography often shows characteristic ring shadows due to distortion of the calyces by the cysts

Course —This closely resembles that of chronic nephritis

Treatment —The treatment is that of chronic nephritis Operation is contra indicated since both kidneys are nearly always equally affected

OTHER FORMS OF CYSTIC DISEASE

Echinococcus cysts may occur in the kidney and the discharge of the daughter cysts has produced attacks of renal colic *Cystic degeneration of renal neoplasms* is described elsewhere

MOVABLE KIDNEY

Synonym —Nephroptosis

The kidney is normally held in place by the perirenal fat the renal vessels and the peritoneum stretched over it But this does not prevent a certain amount of respiratory excursion as may be seen either by radiographic examination or in the operating theatre The range of movement varies between 1 and 2 inches and is more marked on the right than the left side The term movable kidney should there- fore only be applied to cases where there is an excessive respiratory descent so that the upper as well as the lower pole can be felt or where the kidney can be moved

about by external manipulation As the kidney slips downwards the lower pole gradually passes towards the middle line, while the organ rotates slightly, causing the hilum to look somewhat upwards

Ætiology—Movable kidney is about seven times more common on the right than on the left side The ascending colon and the hepatic flexure lie on the inner aspect of the right kidney thus tending to drag it down when the bowel is loaded or dropped On the left side, on the other hand the strong costo colic fold suspends the splenic flexure much more securely while the descending colon lies to the outer side of the left kidney

The condition is much commoner in women than in men In men the kidney pouches are deep narrow and rapidly diminish in breadth from above downwards while in women they are much shallower and broader, and diminish only slightly in breadth from above downwards This natural difference is accentuated in the spare long waisted women with narrow loins who are recognised as specially liable to floating kidney

Pathology—Many reasons have been given for the occurrence of movable kidney, but few will stand investigation Wasting with loss of perirenal fat or loss of tone in the muscles of the abdominal wall have been held responsible but movable kidney is so common apart from such conditions that their importance is doubtful Glénard emphasised the frequency with which movable kidney is associated with a general visceroptosis indeed it is rare to find a movable kidney without coloptosis Movable kidney is the most obvious sign of visceroptosis because the organ is easily palpable

A serious sequel is the occasional occurrence of hydronephrosis produced by torsion of the ureter during the forward rotation of the organ or by its becoming kinked over the renal vessels If hydronephrosis occurs a subsequent infection may convert it into a pyonephrosis

Symptoms—There may be no symptoms at all and if the movable kidney is only discovered in the course of routine examination it is better not to tell the patient of its existence The commonest symptom is a constant dragging pain owing to traction on the renal plexus This most frequently first declares itself between 25 and 35 years of age A zone of hyperæsthesia corresponding to the distribution of the tenth thoracic segment may also be present More serious symptoms directly due to movable kidney are Dietl s crises but these are not common The attacks are characterised by severe pain radiating down the ureter and through to the back and may be accompanied by shivering nausea vomiting fever and collapse The urine is scanty and may contain blood Sometimes the pelvis of the kidney may become distended giving rise to an obvious increase in the size of the organ thus causing a tumour which is easily palpable and may be so large as to be obvious on abdominal inspection This may pass off later with abundant discharge of urine, showing that the crises are due to kinking and consequent partial obstruction of the ureter If repeated they may lead to hydronephrosis The other symptoms which have been attributed to floating kidney are really due to the associated visceroptosis (*q v*) A movable kidney usually feels larger than the normal excised organ This is because of the surrounding investments through which it is felt

Diagnosis—Usually this is obvious as the shape and mobility of the organ are so characteristic Occasionally a Riedel s lobe has been taken for movable kidney but the continuity of the former with the liver should prevent this mistake being made In the same way, a distended gall bladder is continuous with the liver and cannot be separated from it Moreover it is not nearly so movable and curves characteristically towards the umbilicus Carcinoma of the pylorus has offered difficulties in some cases examination of the stools for occult blood a test meal and radiographic examination will clear up the diagnosis Scybala near the flexures of the colon may be mistaken for floating kidney but their indefinite shape and inelasticity

generally help to distinguish them Their disappearance after a series of enemata will settle the question In one case a mesenteric cyst appeared closely to resemble a floating kidney

Prognosis —Apart from the development of hydronephrosis movable kidney does not tend to shorten life in any way It is doubtful whether a kidney once pro lapsed can ever maintain the normal position unaided

Treatment —Some cases call for no local treatment though the associated viscer optosis and neurasthenia will require attention If pain is felt the adoption for a short time of the knee elbow position or simply lying flat on the abdomen will help to replace the kidney and relieve the tension on the renal plexus If pain is at all frequent an abdominal support should be worn namely a corset especially designed to give support to the lower abdomen and increase the general intra abdominal pressure Kidney belts and special pads to support the movable kidney are no good Breathing exercises to develop the expansion of the lower thorax with exercises to improve the tone of the abdominal wall and general measures to improve muscle tone should be prescribed in all cases Treatment on these lines may make the wearing of a special corset unnecessary Operation should not be advised except for recurrent Dietl s crises or when there is evidence of hydronephrosis when nephropexy may be done But even this may not be successful, and ultimately nephrectomy may be required for the hydronephrosis

Treatment of Dietl s crises —The patient is put to bed and is advised to lie on his abdomen or try the effect of the knee elbow position Hot fomentations or a kaolin poultice are applied to the affected side A hypodermic injection of a quarter to one third of a grain of morphine may be required if the pain is severe Usually this is sufficient but should the attack last more than a few hours an attempt must be made, under an anæsthetic to rectify the position of the kidney by manipulation Naturally conditions are unfavourable for nephropexy during or immediately after a crisis because of the congested state of the organ

HORACE EVANS
CLIFFORD WILSON

SECTION XV

DISEASES OF THE JOINTS, FIBROUS TISSUES AND MUSCLES

ARTHRITIS

THE diagnosis of 'arthritis' should be reserved for cases in which there are intrinsic pathological changes in a joint

The clinical conception of chronic arthritis is much simplified by modern classification which divides it into two clear cut *clinical* types, each of which presents distinctive features These are the rheumatoid arthritic type and the osteo arthritic type The features of the rheumatoid and osteo arthritic types of arthritis will be found under their respective headings below, and since the criteria of these types are clinical, this terminology can be correctly employed in those cases in which the ætiology remains obscure

The basic difference between these two types is that rheumatoid arthritis is a general disease in which the most obvious local effects fall upon the locomotor system, while osteo arthritis is a degenerative type of change which without affecting the patient s general health for various reasons becomes localised in certain joints

There are in addition certain cases which are referred to as 'mixed', in which the degenerative lesions of osteo arthritis become superimposed upon those of an inflammatory arthritis of the rheumatoid type

1 RHEUMATOID ARTHRITIS

Synonyms —Atrophic Arthritis Polyarthritis

Rheumatoid arthritis is a general progressive disease affecting principally the joints, which become swollen and painful If unchecked great destruction and deformity results

Ætiology —The malady is said to occur at least three times as frequently among females Women between the ages of 20 and 40 years are most commonly affected and the disease seldom commences after the menopause Predisposing factors exist *in many cases and include infection malnutrition and emotional shock* Focal infection may be present but this is not usually the main causative factor

Pathology —The pathological processes are inflammatory in nature The soft tissues and the white fibrous structures around the joints are the first to be affected The inflammation then spreads to the capsule and synovium and granulation tissue forms in the angle made by the articular cartilage with the synovium The latter then gradually extends inwards as a ring of pannus , covering and eventually replacing the articular cartilage As this happens on both articular surfaces the tendency is for them to adhere especially if the joint is immobilised for long periods and so fibrous ankylosis occurs which in some cases progresses to a bony ankylosis In some cases there is a marked tendency for the development of ganglia and cysts, which are generally in close association with joints or tendon sheaths

There are atrophic changes affecting the skin' subcutaneous tissues muscles ligaments joints and bones This latter condition of generalised osteoporosis shows

as the first *radiographic* evidence of the disease The peri articular swelling can also be seen in outline but actual joint destruction does not occur until considerably later Some degree of patchy recalcification may be observed when the progress of the disease is checked Osteophytes are never found in rheumatoid arthritis but in late cases very considerable disorganisation of the joints takes place and in these areas the bone sometimes gives the appearance of having been dissolved away

The chief pathological change in the blood is an increase in the sedimentation rate of the red blood cells This is an important index of activity and the response of a patient to treatment over a considerable period can be estimated with some accur acy by means of this together with clinical observation A secondary anæmia is usually present in the pre arthritic phase The glucose tolerance of the patient is generally found to be reduced in the active stages of the disease the albumin globulin ratio in the plasma is often reversed

Symptoms —There is in most cases a prodromal period during which the patient loses a considerable amount of weight and fatigue both mental and physical is a marked feature in nearly all cases There may be other symptoms such as paræsthesia Raynaud like phenomena irregular menstruation tachycardia sweating and a second ary anæmia Certain pioneer symptoms are not uncommon and it is of the utmost importance to recognise these amongst them is pain and tenderness of the heads of the metacarpal bones and especially of the second (Morton s disease) Inter mittent attacks of synovitis without apparent cause and affecting tendon sheaths and joints may also occur

The onset of the arthritic phase is often announced by a swelling of the proximal interphalangeal joints of the second and third fingers of both hands It is usually insidious but is acute in about 10 per cent of cases In the case of the former it is not uncommon for the disease to be marked by long periods of low and inter mittent fever The thyroid gland is also sometimes enlarged, and fibrositic pains may be complained of

Wasting of the small muscles of the hands is generally the next event and the fingers tend to fall into the position of ulnar flexion in which they may ultimately become fixed The affection then spreads centripetally towards the trunk involving in turn the wrists (which often become ankylosed) ankles elbows knees shoulders hips and jaw The bilateral and symmetrical way in which the joints tend to be affected is a striking feature of the disease In some cases the spine itself in due course becomes affected

Whenever a joint becomes involved it will be noticed that the muscles which control it particularly the extensors waste rapidly giving rise to the varying flexion deformities typical of the later stages These may be perpetuated by a fibrous anky losis of the affected joints and contraction of the joint capsule Bony ankylosis may follow this stage and when it does so it generally occurs in the wrists and the bones of the carpus in the first place

In certain cases enlargement of the lymphatic glands occurs and even the spleen may become palpable In those cases in which in addition leucopenia is present the condition is known as Felty s syndrome Sufferers with rheumatoid arthritis generally experience considerable pain which interferes with their sleep and this adds progressively to the severity of the condition

Symptoms often clear up if pregnancy or jaundice occurs during the course of the disease but in most cases they return with renewed vigour after parturition Periodical remissions are a well known occasional feature of the disease they may last for months or even years

Prognosis —Under a properly planned and supervised programme about 20 per cent of patients recover A further 50 per cent. show considerable improvement and an additional 20 per cent are improved to some extent leaving 5 to 10 per cent of cases which appear to be entirely resistant to treatment of all kinds With

modern methods of treatment, gross deformity should very seldom occur, even when ankylosis takes place It should be remembered however that in many cases treatment of some sort is required for months or even years, and that relapse may occur even after apparent cure If the disease is not checked, the end result is often complete and painful crippling This sometimes takes place within a very short period, particularly when the patient is young Cases which occur later in life tend on the whole to be less rapidly progressive in their course

Treatment—It is by a careful and intelligent selection and combination of methods suited to the individual patient that the most favourable results will be obtained A period of rest in bed is essential when the disease is progressing rapidly and there is much swelling of weight bearing and other joints

Diet—This should be rich in vitamins, especially the B complex and C, and extra calcium in the form of milk and cheese is advisable It should also be rich in calories, and there is no reason to restrict any particular type of food in this d se

When the sufferer is much underweight and does not return to normal by d tetic means alone, a small dose of insulin (5 to 10 units) may be administered 15 to 20 minutes before two meals in the day, the allowance of carbohydrates being adjusted accordingly

Physical therapy—In the acute phase these are of necessity reduced to sedative applications and gentle movements They may be supplemented by progressively graded ultra violet rays which stimulate to some extent the patient s powers of resistance Later massage, heat and supervised voluntary movements help to relax the muscle spasm, which is often in itself a cause of pain and tends to increase the ultimate deformity

Splints may be necessary at all stages, to prevent contracture and maintain movement in the affected joints

Drug therapy—Anæmia will respond to iron sometimes only when it is administered intravenously and on general principles the patient needs laxatives for constipation and analgesics for the relief of pain and sleeplessness If aspirin or phenacetin is not effective Dover s powder (gr 10 to 15) or codeine phosphate (gr ¼ to ½) may be tried A time honoured remedy is guaiacol carbonate which may be given with aspirin, thus Guaiacol carb gr 8 aspirin gr 4, in cachet form three times daily after food

Phenylbutazone (Butazolidin)—This drug has a powerful analgesic action on many patients with rheumatoid arthritis but in others it appears to be without effect It may be tried in severe cases before resorting to the use of cortisone The dosage should not exceed 200 mg three times a day because of the danger of toxic effects, which include nausea, vomiting stomatitis, œdema, agranulocytosis, hæmorrhages and skin eruptions

Gold is believed by many observers, to be the most valuable drug in the long term treatment of rheumatoid arthritis It appears to cause remissions in a high percentage of cases and is most effective when the onset of the disease is recent and the blood sedimentation rate is high This method of treatment is contraindicated in the presence of renal or hepatic damage diabetes mellitus eczema severe anæmia colitis, pregnancy, hæmophilia or purpura With regard to other cases the dangers of reaction complications and mortality should be taken into consideration There should be a complete blood count blood sedimentation test and an examination of the urine for albumin The main toxic effects are purpura boils, exfoliative dermatitis gastro enteritis and colitis nephritis aplastic anæmia and stomatitis There is however, a negligible mortality attendant upon this form of therapy The patient should not be exposed to strong sunshine or ultra violet light during the treatment for fear of pigmentation ✓

It is well not to administer gold near the period of the menses as skin eruptions are said to be more liable to occur then There are several preparations of gold salts

on the market It is wise always to employ those which are administered intra muscularly Whether they are suspended in an oily or in an aqueous solution appears to be immaterial The initial dose should be 0 01 g and subsequent doses may be 0 02 and 0 05 g This latter dose should not be exceeded nor should the injections generally be given more frequently than once weekly If no improvement follows the administration of 1 0 g of gold it should be discontinued but when the response is good relapse can usually be prevented by prolonging treatment for an indefinite period Injections of 0 05 g are given at 2 to 4 week intervals unless undesirable side effects occur The complete blood count blood sedimentation rate and urine examination for albumin should be repeated at regular intervals during the treatment If toxic effects are produced the injections should be discontinued immediately and on no account should the patient receive further treatment with gold Serious complications such as exfoliative dermatitis will respond to a short course of corticotrophin Dimercaprol (B A L) which is itself toxic need no longer be used for this purpose

Preparations of bismuth and copper have recently been introduced but it is the experience of British workers that they are not efficient substitutes for gold Prostigmine (physostigmine) has also been advocated as an antidote to muscular spasm which is a painful feature of certain cases of rheumatoid arthritis and a cause of increased joint deformities Current opinion in this country is however unfavourable

Vaccine therapy —This form of treatment is claimed sometimes to reduce the activity of the disease particularly when focal sepsis is an important factor in its ætiology The correct dose of the vaccine is probably the lowest which is found to provoke a favourable reaction and not the highest which can be tolerated

Protein shock may be given in the form of intravenous T A B vaccine injections This is a non specific procedure designed to raise the patient s temperature temporarily in the hope of benefiting him subsequently Such treatment should never be undertaken when the patient is in an active phase of the disease Once improvement has started however it may be justifiable to endeavour to speed its tempo by this means Three to five injections should be administered the dose varying according to the age and weight of the patient At least 24 hours of normal temperature should be allowed between the injections which should not in any case be given more frequently than twice weekly

Repeated blood transfusions apart from correcting the anæmia are sometimes of value in retarding the progress of the disease The value of blood from pregnant women for this purpose is being investigated Thyroid in small doses (gr ¼ to ½ twice daily) or iodine may be useful during the menopause

Focal sepsis —It is unwise to embark upon operative procedures while the patient is in a condition of debility or while the disease is running an acute febrile course with marked joint pain and swelling In such patients an endeavour should previously be made to build up the general health If after 4 to 8 weeks no improvement has occurred and the focus is still believed to be of importance cautious measures for its removal may be initiated The patient should in such cases be warned that it is unlikely that the removal of such a focus will cure the arthritis but that his general health and the powers of active resistance will be stimulated thereby The foci of infection which are of particular importance and should always be investigated are situated in the tonsils the nasal sinuses and the teeth but the colon appendix gall bladder cervix Fallopian tubes prostate and bladder should also be investigated If more than one focus of infection is found the one most apparently active should be treated first In cases in which the sinuses and the tonsils both require surgical attention it is important to allow a period of several weeks to elapse between any two operations

The steroid hormones —Cortisone and corticotrophin (A C T H) are not as valuable in the long term treatment of rheumatoid arthritis as first experience seemed to

suggest Suppression of the disease occurs in the majority of cases at the time of administration, but relapse almost invariably follows the withdrawal of treatment A lengthy course of treatment is justified in selected cases with rapidly worsening disease, and cortisone which can be given by mouth is the hormone of choice An initial dose of 100 mg daily, in three divided doses, is gradually reduced to 25 to 75 mg daily over a period of 2 weeks The equivalent amounts of long acting corticotrophin given intramuscularly once daily, are 30 to 60 mg initially, reduced to a maintenance dose of 20 mg Complete prolonged suppression of symptoms cannot always be achieved without the production of side effects These include rounding of the face, obesity, œdema, disorders of menstruation insomnia tachycardia and hypertension Hirsuties, acne, diabetes severe mental changes hæmorrhages and thromboses are less common

A short course of treatment can sometimes be given as an adjunct to physical measures aimed towards rehabilitation Definitive treatment with repeated short courses has proved disappointing Withdrawal symptoms in the form of weakness malaise loss of appetite and depression are common and in some patients they are more distressing than the disease When inflammation is limited to a few joints, the standard methods of treatment can be supplemented by the intra articular injection of small doses of hydrocortisone (compound F) The steroid hormones *should not be prescribed when disability is due to irreversible changes* and they are contra indicated by such conditions as peptic ulceration acute psychosis tuberculosis and severe acute infections They should be administered with caution when there is hypertension, diabetes or severe osteoporosis Patients on steroid hormone treatment must remain under regular observation

2 SPECIFIC INFECTIVE ARTHRITIS

GONOCOCCAL ARTHRITIS

From 1 to 5 per cent of those infected with gonorrhœa develop gonococcal arthritis The disease is also found in babies whose infection occurs at birth In view of the fact that infection due to this cause frequently ends in crippling and bony ankylosis of the affected joints it is important to make the diagnosis at the earliest possible stage If this is done the prognosis is good

The clinical appearance and course of gonococcal arthritis is similar to that of rheumatoid arthritis when the onset of this disease is acute A differential diagnosis may be made from the following points (1) A recent history of gonococcal infection or urethritis Unless specifically questioned patients often omit to mention this (2) The onset of joint symptoms within 3 weeks of such an infection (3) There is a predominance of 3 1 in males unlike true rheumatoid arthritis *As in the latter disease however the malady is often a polyarthritis from the onset* (4) The knees wrists ankles and frequently the plantar fascia are involved in a virulent attack A painful teno synovitis around the wrists and ankles is a common forerunner of arthritis (5) Conjunctivitis and irido cyclitis are not uncommonly associated with gonococcal arthritis

The complement fixation test of the blood is found to be positive in about 80 per cent of cases after the first month and gonococci may in many cases be grown by special methods from samples of the joint fluid affording an immediate confirmation of the diagnosis

Treatment —Although penicillin will invariably cure the primary infection it is less effective in the treatment of gonococcal arthritis and the most favourable results *have been obtained with artificial fever therapy* In the chronic stages it is important to guard against contractures of the affected joints

MENINGOCOCCAL ARTHRITIS

This is not uncommon in the second week of cerebrospinal fever and may be polyarticular or monarticular It closely resembles gonococcal arthritis except that it is generally less severe There is also a milder sporadic form—chronic meningococcal septicæmia—which occurs in the absence of meningitis and which is probably more common than is generally suspected passing as influenza or subacute rheumatism The diagnosis in these cases rests upon the presence of intermittent low fever a rash which may be purpuric and sometimes simulates erythema nodosum and a positive blood culture Leucopenia is usual in this syndrome The patients often seem surprisingly well and complain of little except joint pains Both these types respond well and rapidly to sulphonamide therapy

PNEUMOCOCCAL ARTHRITIS

A polyarthritis of the rheumatoid type is a rare sequel of pneumonia It affects children more commonly than adults An arthritis affecting one or more of the larger joints is somewhat commoner These conditions generally occur subsequent to the stage of pneumonic resolution

Pathology —The joint fluid is in most cases purulent and pneumococci can be found in it except in cases which have received chemotherapy

Prognosis —If the patient survives the pulmonary infection his resistance to the organism is good and joint function is in most cases preserved provided erosion of the cartilage has not taken place

Treatment —Joints affected in this way should be aspirated early and they should be immobilised in light plaster splints which should be removed daily to permit of gentle movement Specific treatment for the pneumonia must be given

ACUTE SUPPURATIVE ARTHRITIS

This is often polyarticular in its distribution and may be mistaken at first for acute rheumatic fever or rheumatoid arthritis It occurs more often in children than in adults

Ætiology —The condition may be a blood borne infection (metastatic) or may arise as an extension from neighbouring areas of osteomyelitis or other infection The former is the more common and may be secondary to a focus of infection in the middle ear throat sinuses or prostate It may also follow the acute specific fevers particularly scarlet fever and septic tonsillitis It has also been reported following meningitis septic endocarditis infected varicosities and burns pyelitis and furunculosis An arthritis following typhoid fever is not generally suppurative but may become so

The organisms which are chiefly responsible are the hæmolytic streptococcus the staphylococcus the pneumococcus the gonococcus and after typhoid *Salm typhi*

Symptoms —These include an acute onset of chills and sweats pyrexia local pain and tenderness in the joints with redness swelling and limitation of movement There is in most cases a high degree of polymorphonuclear leucocytosis

Course —The joint fluid rapidly becomes purulent and extensive damage to the joints occurs if treatment is not instituted rapidly Badly damaged joints generally ankylose ultimately The mortality amongst such cases used to be in the neighbourhood of 20 per cent

Treatment —Treatment with the antibiotic to which the organism is most sensitive should begin as soon as possible and in the case of penicillin or streptomycin it can also be given directly into the joint Pus should be removed by drainage or aspiration When the infection has been controlled impairment of function due to

muscle wasting will respond to exercises and other methods of rehabilitation but orthopædic treatment may be necessary when there are irreversible destructive changes in the joint

TUBERCULOUS ARTHRITIS

Tuberculous arthritis usually occurs in young patients and is an infection from a primary tuberculous focus elsewhere in the body The possibility of an arthritis in a young subject being tuberculous should always be borne in mind and a radiographic examination is of great value in differentiating this type from other varieties The subject is dealt with fully in surgical books to which the reader is referred

Tuberculosis may also be responsible for certain cases of idiopathic polyarthritis

DYSENTERIC ARTHRITIS

A polyarthritis of the rheumatoid type follows bacillary dysentery in about 3 per cent of cases at an interval varying from 3 weeks to several months after the cessation of acute symptoms It may also occur in the course of a chronic ulcerative colitis In some cases the process only affects one joint but in either event the process commences as an inflammation of the periarticular tissues and progressively invades the joint surfaces Suppuration is rare

Treatment should be directed to the dysenteric condition and should be palliative so far as the joints are concerned Severe arthritis due to ulcerative colitis is an indication for colectomy

REITER S DISEASE

This is an illness of undetermined ætiology which is often self limiting and which is characterised by polyarthritis in association with non venereal urethritis and conjunctivitis Attention was drawn to this syndrome during the campaigns in the Middle East where it was not uncommon amongst young soldiers It was originally held to be related to dysenteric polyarthritis but the consensus of opinion now tends towards a virus ætiology (see p 310)

UNDULANT FEVER OR BRUCELLOSIS

A mild polyarthritis due to chronic infection with the organism of this disease is probably more frequent than is usually believed and is commonly seen in Mediterranean countries It is generally associated with myalgia and sometimes with intermittent hydrarthrosis The onset may be acute or chronic and the clinical picture may closely resemble a subacute attack of rheumatoid arthritis The pain is often very acute

The general symptoms are indefinite and multiple and include malaise long continued low grade pyrexia which undulates loss of weight sweating and depression The blood may show a secondary anæmia and a leucopenia The agglutination tests are usually positive if the disease is of some weeks duration but a negative result is inconclusive The only fully satisfactory diagnosis is based on cultivation of the organism which is however very difficult

DENGUE

This disease gives rise to a very acute form of peri arthritis Intense pain and sometimes swelling occur in the tendons and muscles around the joints These

usually disappear when the fever subsides but in the stage of convalescence may recur and last for weeks or months The condition should be differentiated from rheumatic fever from which it differs in being epidemic and in not responding to salicylates

LEUKAEMIA

Acute leukæmia in children not infrequently presents with swelling redness and pain of one or more joints The disease may thus be confused with rheumatic fever or rheumatoid arthritis

DISSEMINATED LUPUS ERYTHEMATOSUS (see p 933)

3 OSTEO ARTHRITIS

Synonyms—Hypertrophic Arthritis Arthritis Deformans Morbus Coxæ Senilis (of hip)

Osteo arthritis is a degenerative condition which affects the articular cartilages and weight bearing surfaces in most cases of the larger joints

Ætiology—The known factors include trauma congenital joint deformity senility certain disorders of metabolism and nervous diseases *e g* Charcot s joint Prolonged toxæmia is occasionally important but there is no evidence that focal sepsis is con cerned in the ætiology of this type of arthritis There may be an hereditary factor particularly in certain cases of osteo arthritis of the hips

The malady tends to occur principally in men over middle life who have led a strenuous life in women it mainly affects the knees and is often secondary to the proliferative synovitis which is often a distressing feature of the menopause

Pathology—The changes which occur in the joint affect primarily the articular cartilage which in the early stages shows grooving and fibrillation starting at the points where the pressure of the opposing surfaces is greatest Later the cartilage may actually wear through at these points and the two bony surfaces come into contact When this happens the constant rubbing of bone on bone gradually polishes and eburnates these areas At the same time a gradually progressive enlargement of the articular surfaces occurs which culminates in the production of lipping and of bony outgrowths from the joint margins called osteophytes These excrescences may in well established cases be easily palpable at the joint margins and are the typical lesions of osteo arthritis No constant changes other than degenerative are found in the synovium

Symptoms—The onset of the disease is insidious The first symptom to be complained of is usually stiffness often accompanied by pain after exertion The site is generally one or more of the larger joints or it may be any joint which is sub jected to particular stresses as the result of the patient s occupation or recreation In the course of time considerable wasting of the muscles controlling the affected joints supervenes The joints therefore tend to become unstable and so liable to further trauma The coarse grating which can be elicited in joints affected with the disease is due to an accompanying teno synovitis and is no measure of the actual damage to the joints themselves When extrinsic joint changes have occurred the patient usually experiences considerable pain particularly on bearing weight The movements of the joint also become much limited on account of spasm of the sur rounding muscles which may in itself be a cause of pain There is generally not much effusion present Occasionally new bone formation may limit the movements of the joint although this is not very common Small rounded bony swellings on the terminal phalanges of the fingers and thumbs termed Heberden s nodes not

infrequently develop during the course of the disease. These may be the cause of considerable pain in their early stages, but, on the other hand they may be quite painless.

The examination of a hip joint affected with early osteo arthritis reveals some limitation and pain on rotation and often also of abduction of the joint some time before the movements of flexion and extension are appreciably interfered with. In addition, it may be found that such a patient when standing does not support his weight equally on both hips in order to avoid pain. Some wasting of the gluteus muscle on the affected side is also evident fairly early. In advanced cases actual shortening of the affected limb occurs either as the result of absorption of the femoral head or from its dislocation upwards. Pain complained of in the knee may in reality be referred from a diseased hip; in such cases if a full examination of the patient is omitted treatment may be directed to the wrong joint. 'Sciatica' is often found to be the result of osteo arthritis of the hip or of the lumbar spine, and is sometimes the initial symptom.

Osteo arthritic changes in the lumbar spine are frequently present without giving rise to symptoms and such changes are often discovered radiologically in the course of an examination for another purpose. The sacro iliac joints are in the same way frequently reported as being the seat of osteo arthritis. Many of these patients are symptom free, while others complain of low backache or sciatica.

The osteo arthritic joint does not ankylose but may become locked as the result of excessive osteophyte formation. In other cases it becomes unstable owing to continued use in the presence of insufficient muscular support due to muscular wasting; in these cases the joint surfaces may ultimately become very disorganised.

When a weight bearing joint is affected the patient suffers great pain on standing and a certain amount of absorption of articular bone may occur resulting in some shortening of the limb.

In some cases the articular cartilage may become fragmented or osteophytes may break off into the joint cavity. In both these circumstances they form loose bodies which give rise to all the symptoms usual in that condition in addition to those of the arthritis.

The general health is not affected unless as the result of enforced inactivity or of pain.

Diagnosis—Unless the observer be a slave to names it must be allowed that it is not always easy to call a case one of pure rheumatoid arthritis or osteo arthritis. But speaking generally, the distinction is a true one and it is important to make it whenever possible. Osteo arthritis is a degenerative condition affecting one or two joints, usually the larger ones. There is generally a history of trauma in the past, or of continued trauma of a minor nature such as some occupational or sporting stress or strain, or a postural defect, or in some cases a sudden increase of weight with resultant strain on the ankles, knees or hips such as may occur at the menopause. Apart from the menopausal group of cases the patient is more often a male and his general health is not directly affected by the disease. Again, the pain is generally relieved by rest.

Rheumatoid arthritis on the other hand is a general disease, the joint changes being a conspicuous part of it. These changes are inflammatory in nature, and trauma is not a marked feature. The onset is in the smaller joints, many of which are generally affected symmetrically and bilaterally. The patient is most often a woman and there are as suggested indications of general ill health and loss of weight which often precede the joint manifestations.

The *radiographic* appearance of a joint affected with osteo arthritis is usually typical. The bone density is unaffected but the joint space is narrowed to a degree which depends upon the amount of erosion occurring in the cartilage. Osteophytes are seen at the joint margins and there is frequently also a deposition of calcium in

the attached ends of certain tendons such as those of the patella and ligaments, *e g* the cruciates which result in an appearance of spiking This is sometimes found independently of the existence of osteo arthritis In osteo arthritis of the hip considerable deformity both of the head of the femur and of the acetabulum may be seen and in addition small degenerative cystic areas adjacent to the joint are not infrequently noticed The radiographic findings are often unrelated to the degree of pain in the particular case, this may be severe with very little radiographic deviation from the normal whereas the grossest radiographic changes are sometimes compatible with little pain

The blood sedimentation rate glucose tolerance test and streptococcal agglutination reaction are normal

Differential Diagnosis —Conditions which are liable to be confused with osteo-arthritis are Paget s disease osteochrondritis dissecans and occasionally neoplastic growths of the articular ends of bones

Prognosis —If not treated the course of osteo arthritis is progressive and generally ends in disablement Much however can be done in the early stage to prevent this by relieving the affected joint of all possible strain and by support and correct treatment The outlook is perhaps best in that form known as menopausal arthritis provided full and adequate measures are taken before the malady becomes firmly established

Treatment —As there is usually an absence of general symptoms there is no indication for general treatment other than seeing that the patients receive an adequate supply of vitamins and that definite periods of rest are secured If the patient is obese a diet low in fats and carbohydrates should be insisted upon if success from other measures is to be achieved The caloric value should not exceed 1600 calories and fluids should not be taken at the same time as food The patients should be reassured that they will not become extensively and hopelessly crippled as may occur in rheumatoid arthritis

It is the experience of most observers that little benefit is to be anticipated as the direct result of removing foci of infection If however these are found they should be dealt with on their merits If varicose veins are present as is often the case when the malady is situated in the knees treatment directed towards these may result in some improvement in the joints

The drugs chiefly valuable in this condition are those of the analgesic group such as aspirin phenacetin and codeine They should not be prescribed as a routine and should only be used when pain is severe Phenylbutazone is very effective in certain cases but must be prescribed with caution 200 to 400 mg daily may relieve the pain and this dose can be maintained over long periods with reasonable safety It can often be reduced to 100 mg daily with equal effect Gold salts are not indicated in this type of arthritis The intra articular injection of hydrocortisone 25 to 50 mg at frequent intervals gives considerable although temporary relief of symptoms in some cases

In cases which arise about the time of the menopause small doses of iodine and thyroid are often of value but should be combined with the other measures outlined particularly those for reduction in weight and muscular re education Central heating in the home is desirable

Physiotherapy of some sort is essential in the treatment of osteo arthritis Heat is required to stimulate the failing circulation locally and to relieve muscle spasm and consequently pain massage to maintain and stimulate the nutrition and drainage of the skin and underlying tissues and movement in order to maintain the mobility of the joint to prevent or repair muscle wasting and discourage the formation of adhesions When dealing with the extremities paraffin wax applied at a high temperature is also useful as a means of applying heat

Movement should if possible be active *i e* special exercises or if this is not

feasible at the outset, electrical stimulation by means of the surging faradic current, or hydrotherapy if available, may be substituted Movement of the affected joint should however, as far as possible be dissociated from weight bearing through the affected joint, in order to allow of repair in the cartilage Where the deep pool or the Guthrie Smith slings are available for this purpose they are helpful

The question of posture, or ' body mechanics ' is an important and neglected aspect in many cases of osteo arthritis For instance, pronated feet may cause strain and later, arthritis, in both knees and lumbar spine as may a pendulous abdomen Proper postural exercises should be taught, and the patient should continue with these until the correct posture is maintained reflexly

When after a period of rest the patient begins to put weight on to the affected joint again the latter should always be adequately supported For this purpose a crepe bandage, or Elastoplast is of great value In some cases special appliances, such as the Howard Marsh splint for the knees or a back support when the spine is affected, may be needed for a period in order to protect the joint For the feet proper arch supports may be necessary while in cases of severe arthritis of the hip or knee when weight bearing continues to give great pain some form of walking caliper, whereby the weight of the body is ' by-passed ' from the ischium down to the heel of the shoe by a light metal rod is indicated

In very advanced cases operative procedures may prove necessary Chief amongst these are synovectomy in those cases in which soft tissue proliferation is not responsive to other treatment When in the hip joint a small degree of painful movement is all that remains possible of achievement arthrodesis either by open operation or by means of the Smith Petersen pin is often the best method of treatment Arthroplasty in experienced hands is a successful operation but old age is a contraindication because of the considerable length of time necessary for rehabilitation Tavernier's operation for section of the obturator nerve if successful is pain relieving

4 HYPERTROPHIC PULMONARY OSTEO ARTHROPATHY (see p 1171)

5 ARTHRITIS DUE TO GOUT (see p 444)

6 SPONDYLITIS

Spondylitis is arthritis of the spine Most cases fall into one of three types (1) the ankylosing type—spondylitis ankylopoietica, (2) rheumatoid arthritis in which the spine is involved as part of the general disease and (3) osteo arthritis of the spine

1 ANKYLOSING TYPE OF SPONDYLITIS

Synonyms—Ankylosing Spondylitis Spondylitis Ankylopoietica Atrophic type of Spondylitis Spondylose Rhizomelique Von Bechterew's Disease Marie Strumpell Disease It is now realised that all these terms apply to the ankylosing type of spondylitis or sub varieties of this

Ætiology—The predisposing and exciting factors are probably the same as in rheumatoid arthritis In America where it is known as Rheumatoid Spondylitis it is believed to be a variant of that disease The age of onset is similar, occurring chiefly in the young but males are predominantly affected The disease is sometimes familial

Non specific urethritis is considered by some authorities to be a cause of ankylosing spondylitis

Pathology—The only true joints in the spinal column are those which permit of movement between the intervertebral articular facets and the costo vertebral joints

This type of arthritis commences as a synovitis of these joints followed by some *osteoporosis of the vertebral bodies and in the majority* of established cases radiological evidence of an infective process will also be found in the sacro iliac joints The ligaments surrounding the affected joints subsequently calcify and those portions of the spinal column become rigid When this process is complete the lateral borders of the intervertebral discs also calcify as do the anterior and lateral longitudinal ligaments the whole process resulting in a bamboo like appearance which is radiologically typical of the condition when fully developed

Symptoms—The early symptoms of ankylosing spondylitis are usually of a diffuse and insignificant nature and are therefore generally overlooked until they become localised in the spine which may be comparatively late in the disease The principal complaint is often of a diffuse fibrositis which chiefly affects the upper part of the body This syndrome if it persists should always arouse a suspicion of spondylitis in the case of a young male In others pain may be referred directly from the affected spinal segment and may simulate that of renal calculus pleurisy or even tabes Sometimes neuritis or numbness and loss of power in the limbs or severe spasm of the muscles of the back may be complained of All these symptoms are usually intensified on forced movement of the spine and in addition pain is often elicited by firmly tapping the spinous processes involved

There is also increasing stiffness in the back and ultimately this may become completely rigid (poker back) generally in a position of kyphosis and slight forward flexion of the spine In untreated cases this position becomes very exaggerated the chin sinks into the chest wall and the patient is unable to stand erect or move Those who are not bedridden move with a characteristic slow bent shuffling gait As the *costo vertebral joints ankylose so does the respiratory expansion of the chest diminish*

Complications—Those who die with this disease generally do so from respiratory infection the result of restricted chest expansion due to ankylosis of the costo vertebral joints The disease in itself does not usually shorten life

Diagnosis—All patients especially young and athletic males who complain of vague pains affecting the limbs and upper part of the body which do not respond *to treatment should be suspect The presence of detectable rigidity of the spine* is unusual at this stage If the blood sedimentation rate is high this increases the suspicion and should lead to the patient being radiographed The radiological appearances at this stage if present are loss of definition (woolliness) of the sacro iliac joints osteoporosis of the neighbouring bones and lumbar vertebral bodies Later the sacro iliac joints become obliterated and the intervertebral joints are hazy and later may be ankylosed The edges of the intervertebral disks and the spinal ligaments are calcified The vertebræ primarily affected are usually those of the lumbar and lower cervical portions of the spine Osteophytes are not found At this later stage the diagnosis becomes obvious as the whole spine is rigid The hip and shoulder joints are sometimes affected

Course and Prognosis—In cases in which the onset is acute ankylosis of the spine may occur within a few months The younger the patient the more likely is this to happen An associated swelling of other joints in the body develops at some period of the disease in about 25 per cent of all cases while the hips and shoulder joints are liable to be permanently involved in about the same proportion of cases Iritis occurs in a significant proportion

Treatment—It should be remembered that spondylitis of this type is a systemic disease and thus needs general treatment as well as more specialised attention to the spine Treatment is more successful if it can be started at an early stage of the disease The general treatment is similar to that advised for rheumatoid arthritis rest and a high caloric diet rich in vitamins Any definite foci of infection should be cautiously removed and anæmia counteracted Ultra violet light is a useful general tonic Gold salts do not appear to be useful in this condition Cortisone and

corticotrophin are of considerable value in suppressing the acute exacerbations The principles of treatment and dosage are the same as in rheumatoid arthritis (p 1152)

In the active stage rest in bed and mobilisation of the chest by means of breathing exercises are essential Fracture boards should be placed under the mattress to prevent sagging and the patient should be as flat as possible, the pillows being removed several times daily in order to hyperextend the spine Better still a plaster cast should be made of the back in which the patient can lie thereby maintaining the natural curves of the spine Breathing exercises undertaken in this position should aim at keeping the chest wall mobile by restricting abdominal breathing Physiotherapy is chiefly of value in the form of radiant heat or infra red rays to the back in order to relax spasm and relieve pain Gentle massage is useful for the same purpose and later active movements should be performed under supervision If there is already some deformity of the spine a plaster shell is essential and the patient should lie in this night and day to relax completely all spasm It should be altered frequently so as to take advantage of the gradual postural improvement, and when the patient first assumes the upright position he should be fitted with a light spinal brace to relieve the back from all strain Special mobilising exercises are indicated when the disease is less active

Radiotherapy to the sacro iliac joints and the spinal column is an important part of the treatment of these cases Its effect appears to be more than merely palliative

Even with the greatest care it is sometimes impossible to avoid ankylosis of the spine But if this does occur it is almost always possible to ensure that it does so in the optimum position and thus the patient will ultimately be able to lead a reasonably active life in an erect posture

2 RHEUMATOID ARTHRITIS WITH SECONDARY SPONDYLITIS (see p 1151)

3 OSTEO ARTHRITIC TYPE OF SPONDYLITIS

Synonyms —Osteo arthritis of Spine, Hypertrophic Spondylitis Degenerative Spondylitis Spondylosis

Some degree of osteo arthritis of the spine is present in the majority of people over 50 years of age, but it is unusual for these changes to cause symptoms Its incidence is rather higher in men than women and it seldom occurs before middle life It often follows trauma

Pathology —The changes are not inflammatory in nature and are identical with those of osteo arthritis met with elsewhere in the body Bony ankylosis does not occur in this type of arthritis but osteophyte formation is always seen together with narrowing and degeneration of the intervertebral spaces The areas most commonly involved are the cervical and lumbar regions and in the former protrusion of the intervertebral disks may result in spinal cord and nerve root compression

Symptoms —When symptoms are present they may include the following root pains of which sciatica is the most frequent example increasing stiffness of the back which however never becomes completely rigid Headache and pains in the neck shoulders and arms are common sometimes in conjunction with areas of paræsthesia or anæsthesia in the skin Pains are generally aggravated by movement of the spine, as the nerve roots are liable to pressure in or around their exit from the spinal foramina Cervical spondylosis may cause paraplegia due to ventral compression of the spinal cord a Brown Sequard syndrome due to lateral compression of the spinal cord and radicular symptoms when nerve roots are involved

Diagnosis —This should be confirmed radiologically The lesion typical of osteo arthritis is the osteophyte while marginal exostosis and shrinking of the vertebral margins with narrowing of the intervertebral spaces are also seen The sacro iliac joints are generally normal In all cases the possibility of malignant growths

or Paget s disease in the spine should be borne in mind as the symptomatology may be the same Myelography may be required to establish the diagnosis in doubtful ca es

Treatment —This i similar to that of osteo arthritis elsewhere in the body and includes the correction of body posture and flat feet The frequent application of heat in some form followed by rest and muscular relaxation is important Massage and faradism at a later stage helps the muscular support of the back Sometimes it is necessary to supplement the support of the back mechanically by a plaster cast or a brace Radiotherapy sometimes relieves intractable pain which proves resistant to analgesic drugs such as aspirin phenacetin codeine or phenylbutazone Conservative treatment of cervical spondylosis with neurological complications consists of bed rest physiotherapy and the immobilisation of the head and neck by means of a collar support Surgical treatment is confined to laminectomy because the offending osteophytic ridge is anterior to the cervical cord and is therefore inaccessible

7 STILL S DISEASE

This disease is believed by most observers to be the juvenile form of rheumatoid arthritis But although the articular changes are of an inflammatory nature their effects are more often confined to the periarticular tissues Again even in cases of long standing it is not unusual to find little or no radiological evidence of destruction at the actual joint surfaces

Ætiology —The sexes are affected in about equal proportion while the age incidence resembles that of rheumatic fever Thus the malady is seldom met with before the age of 3 years and the average age at onset is between 6 and 7 years The cause remains unknown although the factors held to be responsible for rheumatoid arthritis are usually invoked to account also for Still s disease These are focal infection metabolic or endocrine disorder or in some cases unsuspected and attenuated infection with the tubercle bacillus In the majority of cases it is very difficult to assign any one cause It is certain however that once the disease has commenced a cold damp environment exacerbates it considerably

Symptoms —If a careful enquiry of the history of the patient s illness be made it is often found that a considerable period of prodromal ill health preceded the onset of the joint symptoms

The onset of the joint condition is not infrequently rapid with pyrexia and pain and swelling of several joints This often leads to an initial diagnosis of rheumatic fever but it is soon found that sodium salicylate has no beneficial effect and that the joint swellings far from being transient increase in number and intensity When the onset is gradual there is little pyrexia but a slowly progressive degree of swelling and limitation in movement of the knees wrists elbows fingers and ankles—usually in that order Later the cervical spine and also the hips may become affected and the patient becomes completely crippled The foregoing joints are usually attacked symmetrically and their appearance is characteristic in that the periarticular swelling renders the joint fusiform in shape The skin over this swelling is rather stretched and often slightly bluish The muscles adjacent to the affected joints waste which further exaggerates the fusiform appearance In the case of the wrists ankles and elbows the bony contours are often completely obscured The affected joints are generally tender on pressure but usually are not painful except on movement This leads to further voluntary limitation of movement and so intensifies the muscle wasting already present

In many cases of this disease the joint swelling and muscular wasting are accompanied by a lymphatic reaction which shows as enlargement of the superficial lymphatic glands especially those around the elbows and in the axillæ In about half the cases

seen there is also enlargement of the spleen These changes were present in the cases originally described by Still in 1897 The enlarged glands are not tender and are generally discrete and ' rubbery Subcutaneous nodules are sometimes found in addition

There is generally a secondary anæmia, and quite often patches of light brown pigmentation on the skin When the disease is established the extremities are cold and clammy, and there is an increase in the temperature before other joints are affected In long standing cases normal growth is considerably interfered with

In the late stages the type of deformity seen in adult rheumatoid arthritis develops There is flexion of the fingers and ulnar deviation of the hands and also flexion of the knees and elbows

The radiographic picture is chiefly remarkable for the advanced degree of the osteoporosis which occurs There are often little or no actual joint changes, and osteophytes are never found

The end result, so far as the joints are concerned, is a fibrous ankylosis or a fibrosis of the joint capsule which is sufficiently complete to resist all attempts at movement of the joint

It is stated that at post mortem examination diffuse pericardial adhesions and adhesive mediastinitis are often discovered although unsuspected during life and evidence of valvular disease of the heart has occasionally been reported

Prognosis —Until recently there was considerable doubt as to what was the ultimate fate of these patients Some authorities held that they recovered while others explained the rarity of the affection in adult out patient departments by assuming that the patients either died or became rapidly bedridden after leaving the children s departments In one series the mortality in those under 5 years of age was about 25 per cent (due to intercurrent infections) complete recovery occurred in a small proportion while in the majority the disease remained apparently arrested often for several years at a time only to resume its ravages at increasing intervals until the patients were entirely crippled and bedridden

Treatment —When the presence of an infective focus is established this should be dealt with at an early stage of the disease In all cases the child s resistance should be built up by all available means A nourishing diet an open air life and a dry sunny climate are indicated In addition cod liver oil and malt syrup of iodide of iron, and courses of an arsenic containing tonic are important Salicylates have little or no beneficial effect Non specific protein therapy is often recommended but is too drastic and temporary a measure to employ except in the later stages Good results have occasionally been reported from small doses of gold salts administered intra muscularly in short courses But in some cases these salts provoke unfavourable reactions and so should be used very cautiously No case should receive a larger dose than 0 05 g and a total course of 0 5 g should rarely be exceeded The in jections should be given at fortnightly intervals, and the onset of toxic nephritis, stomatitis diarrhœa and dermatitis should be especially looked for The response to cortisone and corticotrophin is the same as in adult rheumatoid arthritis The initial response is generally excellent but as treatment may have to be protracted the likelihood of toxic effects is thereby increased

All swollen joints should be bandaged and lightly splinted or put into thin plaster of Paris casts to avoid the contraction deformities which otherwise inevitably occur The child should always sleep in these and soon becomes accustomed to them They should be removed daily however for a short period, during which the joint must be given active assisted movement to prevent fixation Dry heat from a radiant heat or infra red ray lamp is comfortable and renders the performance of these daily active movements easier These movements are also essential to remedy the muscular atrophy present Massage is generally unnecessary in these cases

In the very late stages, when the patient is bedridden owing to extensive contrac-

tion deformity minor surgical procedures such as tenotomy, are justifiable to remedy the deformity

PSEUDO ARTHRITIS (SYNOVITIS)

Effusion of fluid into the joints may be associated with various conditions and is often of a temporary or intermittent nature

Apart from the various forms of true arthritis already described the following may give rise to joint effusion

(i) *The specific fevers* especially scarlet fever meningococcal fever puerperal fever syphilis typhoid or paratyphoid fever yaws and malaria In the United States a form of pseudo arthritis associated with lymphogranuloma venereum is not un common

(ii) *Abnormal blood conditions* such as purpura simplex or purpura rheumatica (Schonlein s disease) scurvy and hæmophilia give rise to swelling of the joints due to an effusion of blood The knees are most frequently affected

(iii) *Growths affecting the bones* in near proximity to a joint

(iv) *Injection of animal sera* *i e* apart from serum sickness arising on the seventh to tenth day after the u e of foreign serum in treatment

(v) *Trauma* may cause synovitis or hæmarthrosis of the affected joint It should be noted that the strain imposed on certain joints due to faulty body posture occa sionally results in a chronic form of hydrarthrosis

(vi) *Intermittent hydrarthrosis* a periodic recurrence of joint effusion of unknown ætiology which persists for several days and usually affects the knees Attacks tend to recur at regular intervals they show no local evidence of inflammation and they are refractory to most forms of treatment This condition is probably the result of an allergic sensitisation and treatment should be directed along these lines It may represent an atypical form of onset of rheumatoid arthritis

(vii) *Palindromic rheumatism* —This is a form of recurrent painful swelling of the joints which shows intense inflammatory synovial reaction It has been exhaustively investigated by Hench but the cause remains unknown

NON-ARTICULAR RHEUMATISM FIBROSITIS

Non articular rheumatism and fibrositis are the terms employed to designate pain which is situated in the soft tissues of the limbs or trunk and of which the causation is obscure It is accompanied by muscle tenderness and spasm but there is no deterioration in the general health of the sufferer A feature of the classical type is that the pain can often be shown to originate in nodules which are acutely tender to pressure and from which the general pain is referred

In view of the obscurity which at present shrouds its true nature it can perhaps be best classified according to the part of the body which it affects *e g* fibrositis of the head and neck brachialgia intercostal fibrositis fibrositis of the back (lumbago) etc It may also be subdivided broadly according to the nature of the structures which appear principally to be affected *e g* *Panniculitis*—inflammation (or increased tension from some cause) of the deep subcutaneous fat *Peri arthritis*—inflammation of the structures surrounding joints (including bursæ) *Peri neuritis*—inflammation of the nerve sheath and fibrous tissue between the nerve fibres Considerable doubt has however been cast in recent years upon the occurrence of the latter as the result of rheumatism

Ætiology —Fibrositis can sometimes be attributed to focal sepsis particularly of the teeth tonsils nasal sinuses and prostate

A further group of cases would appear to be of metabolic origin *i e* allied to gout or to a special sensitivity to certain types of food It may sometimes be the outward manifestation of mental anxiety or tension and in America the term "psychogenic rheumatism" is much employed

Finally a certain proportion of cases of fibrositis can be traced to chronic strain often secondary to faulty posture A common example of this will be found in those cases in which the fascia lata is tender and painful in conjunction with a flattened plantar arch Such patients are usually cured when the distribution of the body weight is readjusted by raising the inner edges of the shoes Some cases of low back ache seem also to be attributable to the same cause

Morbid Anatomy—This was investigated originally by Stockman who believed that the results of injury to fibrous tissue, whether bacterial or traumatic had the effect of producing in the acute stage an exudate and inflammatory œdema As the condition becomes chronic there is said to be a production of dense connective tissue in nodules or strands, which differ from normal fibrous tissue in having more fibroblasts In 1944 Copeman and Ackerman produced evidence based upon biopsy, that certain cases of fibrositis are caused by a non inflammatory œdema of fat lobules which are invested with a non distensible fibrous fascia This increase in tension appears to be the cause of the pain In later stages the lobule may actually herniate through a weak spot in its fascial covering producing a tense palpable nodule

F A Elliott has suggested that in some myalgias and also in some cases of "fibrositis" local areas of tenderness or 'nodules' may be the result of muscle spasm centrally induced through irritated nerve roots

Symptoms—The pain complained of in fibrositis is not always at the real seat of the lesion but may be referred from other areas and therefore careful location of the actual seat of the inflammation is essential Again, the symptoms vary according to the area of the body affected As examples the predominant effect of involvement of the muscles of the neck is often headache, of those of the limbs numbness and tingling and of the fibrous tissue surrounding joints stiffness and pain on moving these often wrongly attributed to true arthritis

Panniculitis is met with most typically in the early stages of ' menopausal arthritis in which tender pads of thickened adipose tissue are found over the internal aspects of the knees the back of the neck the extensor surfaces of the arms the outer aspects of the thighs and elsewhere It occurs most frequently in stout people, and Dercum s disease or adiposis dolorosa is an extreme degree of this process In some cases this syndrome appears to be associated with moderate hypothyroidism Nodules which are not tender, are often felt in these and other patients

Lumbago is perhaps the most common manifestation of fibrositis Its onset may often be very acute It should be distinguished from arthritis neoplasm or caries of the spine sacro iliac disease, perinephric abscess and renal disease all of which may simulate it *Sciatica* is in a majority of cases probably due to a central lesion of one of the lumbar nerves often a prolapsed intervertebral disk neoplasm or inflammatory lesion (see p 1581) It must not be forgotten however that an appreciable number of cases remain in which the lesion is due to fibrositis *Pleurodynia* is a rheumatic inflammation of the intercostal muscles which gives rise to severe pain when the affected muscles are brought into action as on coughing or deep breathing Usually local tenderness can be elicited on palpation but careful examination is needed to exclude such sources of pain as pleurisy, cardiac disease intercostal neuralgia or prolapse of a thoracic intervertebral disk These muscles are also affected in epidemic myalgia (Bornholm disease) The extensor region of the thighs when they are the seat of rheumatic lesions give the clinical appearance of sciatica and this possibility should always be considered before making a diagnosis

Brachial neuritis—Brachial neuritis in its strict sense is usually an ill founded diagnosis though acute infective radiculitis is a genuine entity The commonest

cause of severe bilateral brachial neuritis is a cervical intervertebral disk lesion unilateral brachial neuritis is frequently due to supraspinatus tendinitis which is often the cause of inflammation of the subacromial bursa through which this tendon passes Another group of causes of brachial neuralgia are the cervico brachial syndromes which include the compression of vessels or nerves at the thoracic outlet by a cervical rib or an abnormally placed clavicle or a spastic scalene muscle (acro paræsthesia) These are all dependent upon a mechanical factor of some sort (see pp 1577 1579) Tennis elbow is the term applied to the painful fibrositis affecting the origin of the extensor tendons of the forearm from the external condyle of the humerus

Bursitis may occur in any of the large bursæ The most commonly affected is the subacromial bursa referred to above The chief clinical manifestations of deltoid bursitis are great pain on actively abducting the affected arm to an angle of 90 with the body Above this point abduction can generally be completed without pain the pain returning however at the same point when the arm is again lowered Passive movement through this range is not painful Pain of this type encourages the sufferer to immobilise the affected arm and this allows the inflammation to spread to the joint capsule which contracts and ultimately limits or even entirely prevents movement in the joint This *frozen shoulder syndrome is not* an infrequent late complication of cardiac infarction The patient is often unaware of the full degree of limitation of the movement which has occurred in such cases as a considerable degree of movement is possible by virtue of the mobility of the scapula This condition is the severest type of peri arthritis and the apparent ankylosis of the joint must be differentiated from a true arthritis by means of radiography as peri arthritis of this type may be cured by the employment of diathermy with active assisted movements and remedial exercises or if the diagnosis is clear and these means fail by manipulation under anæsthesia The bursæ next most commonly affected are those over the olecranon process around the knee joint over the ischium and over the great trochanter Inflammation of any of these should be differentiated from a true arthritis of the neighbouring joint Another form of peri arthritis depends on inflammation of the tendon sheaths of muscles surrounding joints This may occur as part of a chronic rheumatic process unassociated with trauma or gout Its association with gonorrhœal and dysenteric infections has been mentioned The flexor tendons of the wrists and knees are the most commonly attacked Pain swelling or crepitus results and sometimes synovial effusion Occasionally the extensor tendon of the thumb alone becomes painful and thickened resulting in a loss of abduction and great tenderness and thickening This is referred to as stenosing tendovaginitis (De Quervain s disease) and is brilliantly amenable to operative treatment

The palmar fascia is sometimes the site of a chronic fibrositic process and the resulting thickening and contracture is known as *Dupuytren s contracture* This is seldom painful but can give rise to considerable disablement of a somewhat intractable nature The condition which is much commoner in males than in females is often found to be familial A somewhat similar condition which however does not cause so much contracture is known as painful heel In some cases a small spur of bone is found radiographically at the insertion of the plantar fascia into the os calcis though spurs may also be found in subjects who are free from the condition But in the majority of cases no cause for the pain can be found

The subjects of fibrositis are usually found to have some degree of defective skin circulation as evidenced by abnormal sensitivity to cold weather or to local draughts spontaneous bruising or the fact that they perspire in the hottest weather only with difficulty Attacks of fibrositis occur in many people without apparent detriment to their general health

The group of cases which appear to be allied to gout or to a special sensitivity to certain types of food may be suspected by the excellent general health even during

attacks the periodic or seasonal nature of the attacks a history of familial gout or of being "unable to digest certain foods or drinks and finally by the fact that the fibrositis tends to affect the lower limbs and other lower parts of the body Such patients in addition often exhibit the symptom complex described by the French as hépatisme' This is shown principally by morning headache furred tongue and a tendency to incomplete bowel emptying with light coloured and offensive stools, often too, there is slight tenderness on palpation of the liver

Prognosis—Provided sufficient care be taken and the value of external as well as internal remedies is remembered, the outlook is good An exception, however is in the case of old patients for the senile form of fibrositis is sometimes intractable to all the usual remedies

Treatment—When symptoms do not call for urgent treatment, the first indication is to investigate the ætiology In the majority of cases in which the malady is believed to be allied to gout or due to a special sensitivity to certain types of food appropriate treatment should be adopted

At the outset, a mercurial purgative such as calomel (gr ¼ to 2) followed next morning by a saline should be prescribed In the acute stage rest in bed is desirable The internal administration of analgesic drugs is indicated Aspirin and calcium acetylsalicylate (gr 5 to 15) are in the majority of cases the most efficient for this purpose If necessary potassium iodide (gr 2 to 5) may be added as may phenacetin (gr 5 to 10) or caffeine (gr 5) at 4 hourly intervals A useful addition to aspirin and phenacetin is codeine phosphate (gr ⅛) or Dover s powder (gr 5 to 15) Phenyl butazone (200 to 600 mg daily) is sometimes effective An ointment designed to act either as a rubefacient or as a counter-irritant should also be prescribed In acute cases a hot linseed or kaolin poultice will often give considerable relief if applied every few hours as may a hot cloth wrung out of a solution of ordinary mustard in water Massage is undesirable in the acute stage In certain cases benefit will result from a short course of colonic lavage twice a week for 2 to 3 weeks

When it is desired to immobilise the muscles of the back during the acute stage of lumbago the most effective method is by means of a perforated belladonna plaster which should be made to cros the mid line behind and come round to the front *Ordinary wide strapping is a good substitute When the condition is less acute* and the patient is able to get up the application of both heat and massage to the affected regions is indicated The former may be applied in a dry or a moist form the one often succeeding when the other has failed Dry heat may be given by means of a portable lamp, an electric heating pad exposure to a gas fire (which gives out infra red rays) the application of a hot iron through brown paper applied to the skin a hot water bottle or a bag of salt or sand which has been heated thoroughly in the oven When the condition is deep seated diathermy is the best form in which to apply heat

Moist heat may be applied in the form of bread or linseed poultices kaolin poultice (Antiphlogistine) mud packs or applications of hot paraffin wax of a special melting point (which is sold for this purpose) or if the patient is in a condition to have it a Turkish bath Perhaps the simplest method of applying moist heat is in an ordinary bath to which 4 lb of Epsom salts (or common salt) have been added It should be taken as hot as possible and contrary to the general belief the patient should not soak in it but should get out after only 10 minutes immersion and be briskly rubbed down after which some analgesic ointment should be rubbed rapidly into the affected areas and he should be wrapped in a blanket and put to bed for several hours After this deep massage should be ordered for the affected areas although this may be painful at first

Hydrotherapy and counter irritation—When the patient is near a spa or an institution equipped for hydrotherapy spray douche massage followed by contrast douching (alternate hot and cold water directed on to the painful areas under pressure

from a hose pipe) is probably the best follow up treatment it stimulates the skin and muscles to resume their normal functions

In certain cases particularly when the complaint is that of lumbago counter irritation by means of a cautery may be of great value A small blister should result from each application and the whole area may then be covered over with a gauze dressing Another method is to produce blisters by means of blistering fluid or cantharidin plasters but these are not of such value as the actual cautery Dry cupping is a somewhat obsolete method of treatment but is occasionally effective as is full exposure to a Kromayer mercury vapour lamp

In the chronic stage massage is essential if an attack is to be terminated in the minimum time and also if recurrence is to be avoided To be effective the indurated areas (nodules) should be carefully sought for in the muscles and at these points the massage should be deep It will be found that following deep kneading with the finger tips or thumbs after an initial period during which the nodules may be increasingly painful they will gradually become insensible to palpation and ultimately disappear This process will be considerably facilitated if it be preceded on each occasion by 20 to 30 minutes application of heat in one of the forms mentioned above In certain cases a nodule will prove to be too painful for deep massage treatment which will then induce protective spasm in the surrounding muscles and so render further kneading impossible In such cases a dose of aspirin or some other analgesic may usefully be administered before beginning the treatment When one or more discrete trigger points or nodules can be localised and when the pain is referred from these sites the effect of injecting a few millilitres of a local anæsthetic such as procaine hydrochloride (½ per cent in saline) or A B A compound with saline under pressure is sometimes dramatic When there is diffused pain and tenderness this method of treatment is not of much use and unless the injection is made with great accuracy into the nodule the trouble may even be exacerbated There is no doubt however that to achieve a quick result even if it does not prove to be permanent this is the method of choice

Diet and after care —If obesity be present this should be treated (see p 450) In cases in which a gouty origin is suspected this should be corrected (see p 448)

After an attack of fibrositis it is important that the patient should be taught to contract the affected muscles daily by means of appropriate exercises He should also make a point of obtaining some regular exercise in the open air, even at the cost of rising somewhat earlier in order to walk part of the way to the office The obese subject must not be allowed to regain his lost weight once the attack recedes and occupations or hobbies known to precipitate the attacks must be avoided

MYOSITIS OR INFLAMMATION OF THE VOLUNTARY MUSCLES

Three forms occur—(1) the suppurative type (2) the non suppurative type and (3) myositis ossificans progressiva

1 Suppurative Myositis —In this condition there is a primary inflammation of the affected muscles associated with the local signs of inflammation and the general symptoms of a septic infection Abscesses form in the affected muscles which may require incision and in the pus obtained pyogenic organisms such as staphylococci or less commonly streptococci are usually found

2 Non Suppurative Myositis —It must be remembered that the voluntary muscles are affected in the course of several diseases Thus degeneration of the striped muscle known as Zenker s degeneration may occur in any acute infection of long duration it was first observed in typhoid fever In scurvy intra muscular

hæmorrhages are common and these may be followed by a chronic inflammation which usually resolves but in a few such cases suppuration occurs Trichiniasis is accompanied by myositis set up by the encapsulated larvæ of the *Trichinella spiralis* deposited in the voluntary muscles

Dermatomyositis see p 936

3 Myositis Ossificans Progressiva —This is a progressive inflammatory affection of the locomotor system of unknown origin characterised by the deposition of bony substance in the fasciæ muscles aponeuroses tendons, ligaments and bones with resulting ankylosis of the affected articulations The disease is rare It usually commences in early life and is commoner in males Three stages occur in the muscle changes In the first stage swelling and infiltration of the affected muscle *with embryonic connective tissue occurs In the second stage the embryonic* connective tissue becomes organised and forms ordinary connective tissue, which retracts to a hard fibrous mass In the third stage calcification of the fibrous mass occurs and this becomes replaced by bone

The muscles of the back and neck are usually the first to be involved The vertebral ligaments become ossified and the irregular bony swelling produced causes deformity and fixation of the spine The upper and lower limb are later involved the muscles contracting and causing fixation of the joints Finally, the muscles of mastication are affected and this prevents movement of the lower jaw The patient becomes helpless and bedridden, and usually dies from some intercurrent infection, such as pneumonia or pyæmia resulting from bed sores The disease is always progressive but is usually of long duration, and there may be a cessation in its progress for several years No specific treatment is known

W S C Copeman

SECTION XVI

DISEASES OF THE SKELETON

DISEASES of the skeleton will be considered under three headings according to whether bone cartilage or bone marrow is primarily affected

DISEASES OF BONE

HYPERTROPHIC OSTEO-ARTHROPATHY

Synonyms —Hypertrophic Pulmonary Osteo arthropathy Secondary Hyper trophic Osteo arthropathy Marie s Disease Bamberger Marie s Disease Acropachy Simple clubbing is sometimes referred to as Hippocratic Fingers

Definition —A symmetrical enlargement of the bones of the hands and feet and of the distal ends of the long bones accompanied by clubbing of the fingers and toes and sometimes by joint swellings occurring in association with certain chronic diseases especially of the chest and abdomen Clearly simple clubbing of the fingers which is a common phenomenon exists in countless patients without advancing further to produce hypertrophic osteo arthropathy which is rare

Ætiology —The disease is eight times more common in males than females It may occur at all ages including childhood The most striking examples are seen from 30 to 50 The primary diseases in the course of which hypertrophic osteo arthropathy may develop are

1 Diseases of the lungs such as abscess of the lung empyema bronchiectasis carcinoma of the lung and mediastinum or endothelioma of the pleura The condition is rarely seen in cases of pulmonary tuberculo is or non tuberculous fibroid lung

2 Congenital heart disease and infective endocarditis Here there is clubbing of the fingers but the bones are not affected

3 Diseases such as dysentery idiopathic steatorrhœa subphrenic abscess pyelo nephritis polycythæmia rubra vera and hypertrophic cirrhosis of the liver

4 In 10 to 15 per cent of cases the most minute search may fail to reveal a primary cause for the disease Such cases may be familial

5 Pressure on the brachial plexus by a subclavian aneurysm has been known to cause the disease which is then unilateral and confined to the upper limb concerned

Pathology —The bones most frequently affected are the metacarpal bones and the first two rows of phalanges There are no bony changes in the terminal phalanges the soft tissues and nails alone being involved The radius and ulna may be affected and more rarely the lower ends of the humerus and femur the scapula patella iliac crests nose and malar eminences Radiographic examination shows a thin layer of newly formed bone beneath the periosteum which is raised unevenly so that its outline appears serrated and the deposits beneath it are unevenly calcified giving a lace work effect

Symptoms —The onset is usually gradual with little pain though stiffness and clumsiness of movements occur Sometimes marked clubbing of the fingers develops in a few weeks but usually several months or more elapse before the condition is characteristic There is a remarkable symmetry in the pathological changes The ends of the fingers and toes may be cyanosed The nails are large broad and curved

both longitudinally and transversely—the so called parrot beak or drumstick They show longitudinal striation and are brittle and easily split The root of the nail is raised above its bed and if pressure is applied at the root a distinct space between them can be made out The hands and feet become greatly enlarged owing to the bony changes and thickening of the soft parts The forearms and legs are thickened The pelvis sternum ribs and clavicles may be thickened and the vertebræ may show changes resulting in kyphosis Swelling of the joints occurs in about a third of all the reported cases and in practically every one of those in which the process is of long standing The joints involved are those in the neighbourhood of the bones affected, particularly the knees ankles and wrists The lesions are not confined to the synovial membranes and periarticular tissues but may progress to erosion of the articular surfaces Acute painful swelling of the joints occurs especially in cases of endothelioma of the pleura

Diagnosis—The disease is recognised by the presence of the characteristic changes in the extremities and by the presence of signs of one of the primary diseases already mentioned

Acromegaly is to be distinguished by the spade like hand the spatulate fingers enlarged knuckles and the characteristic facial appearance The kyphosis is more often cervico dorsal whereas in hypertrophic pulmonary osteo arthropathy it is more often dorso lumbar

Osteitis deformans shows irregular enlargement of the bones but there is a good deal of bowing the hands are normal and the radiographic appearances are pathognomonic

Rheumatoid arthritis is distinguished by the involvement of the joints of the fingers the absence of clubbing and the changes shown by radiographic examination

Prognosis—Where successful treatment of the primary disease is possible simple clubbing of the fingers may disappear entirely This commonly occurs in empyema and subphrenic abscess In a similar way regressions can occur both in the soft tissues and in the periosteal changes in hypertrophic osteo arthropathy In some cases however cure or arrest of the primary lesion may have no effect on the osteo arthropathy Many cases progress unchecked until they show extreme changes in the skin nails soft tissues bones and joints A considerable degree of ankylosis of the knees sometimes occurs

Treatment—This should be directed towards the cure or improvement of the primary disease Other treatment is symptomatic Care should be taken to avoid ankylosis of the knees at an awkward angle

OSTEITIS DEFORMANS

Synonym—Paget s Disease of Bone

Definition—A chronic and somewhat rare disorder causing enlargement and deformity of many bones It is not a generalised disease of the skeleton The bones are affected in the following order of frequency pelvis spine femur tibia skull fibula clavicle, humerus radius and rib In a few cases the disease is confined to one bone or to part of one bone tibia femur clavicle a vertebra the ilium or half the pelvis

Ætiology—This is unknown The disease is sometimes familial It rarely begins before the age of 40 and the commonest age of onset is 55 The sexes are affected in the proportion of 3 men to 2 women Osteitis deformans is not inflammatory in origin It seems likely that it is a disorder of mineral metabolism Syphilis is not an ætiological factor No alteration in the parathyroid glands nor in any other endocrine gland has been demonstrated Both histological and chemical investigations

have proved beyond doubt that generalised osteitis fibrosa (hyperparathyroidism) is unrelated to osteitis deformans

Pathology —There is a great alteration in the architecture of the bones affected They become enlarged irregularly thickened and sometimes bowed The skull is very thick the sutures and foramina being narrowed in consequence The cortex of the long bones ceases to be pure ivory bone but looks coarse and spongy with red streaks and dots Histologically there is continuous excessive resorption of bone associated with an increased new bone formation that more than compensates for the bone lost The excessive erosion disturbs the skeletal architecture the compact bone being replaced by irregular angular trabeculæ which also form the cancellous bone There is still an attempt at structural adaptation to stresses but this is very imperfectly achieved because the material is not used to the best mechanical advantage

Biochemistry —The serum calcium and plasma phosphorus are normal The plasma phosphatase is constantly high as in many other diseases of bone In more than 80 per cent of cases the calcium output in the urine is increased and sometimes reaches four or five times the normal figure There seems to be a complete absence of correlation between the length of history the density of bone shadows in radio graphs and the calcium output A case showing increased density of bone trabeculæ throughout pelvis lumbar spine and femora is just as likely to reveal a high output of calcium in the urine as a low output

Symptoms —The disease may remain symptomless for 10 years or more It is very slow in progress and rarely influences the general health giving rise in most cases to few symptoms other than those which are due to changes in the shape of the bones In 80 per cent of cases there is pain and the patient usually recognises its origin in the bones It varies widely in severity from a dull ache to a severe shooting or stabbing like a knife The back and lower limbs are the parts usually affected but headache is fairly common When the skull is involved the patient may have to take a larger size in hats The enlargement in the circumference of the head leads to the forehead being prominent and the face small in proportion In the later stages the head is held forward and the back is so bent that the arms appear too long and an ape like attitude results There may be considerable reduction in total height The lower limbs especially are bowed the knees being widely separated and held slightly flexed The bones are enlarged and bowing usually takes place in such a manner as to accentuate the normal curve of the bone The enlargement is particu larly noticeable in the case of the tibia The changes in the vertebræ may cause encroachment on the spinal canal resulting in compression paraplegia Bony com pression of the optic nerve may lead to optic atrophy and of the oculo motor nerves to diplopia Otosclerotic deafness is common in advanced cases Spontaneous fracture is rare but when it takes place there is no delay in union Osteogenic sarcoma may occur but is much less common than Paget thought and is not seen until the changes in the bones have been present for 10 years or more Osteo arthritis of the hip knee ankle or spine is an occasional complication Arterial degeneration some times with hypertension is found in most cases over the age of 50 It is possible that the excess of phosphoric esterase in the blood accelerates and intensifies the deposition of calcium salts in degenerate vessels Retinal arteriosclerosis is a frequent finding and it may be associated both with retinal hæmorrhages and extensive choroidal changes

Radiographic appearances —The altered bone appears in radiographs in two forms which may be called the spongy and the amorphous the former being the more com mon The two types are often found in the same patient The spongy form consists of coarse irregular striæ arranged either as parallel trabeculæ or running in the direc tion of normal lamellæ of cancellous bone The amorphous form is a generalised deposit producing an opaque finely granular appearance The diameter of the bone is increased sometimes to a marked degree and in the medullary cavity the trabeculæ

are accentuated and too widely separated giving a streaky appearance The corticalis is partly or entirely replaced by bone similar to that seen in the medullary cavity, and in an extreme case the *impression is that the whole bone consists of cancellous* tissue highly magnified Irregular cyst like areas are sometimes observed Widening and bowing of bones are important points in the radiological diagnosis The vault of the skull is thickened, and the differentiation between the inner and outer tables is lost Small islands of dense bone are evident alongside pale cyst like areas A large clean cut area *osteoporosis circumscripta* may sometimes be noted In those cases in which part of one bone is affected there is a definite line of demarcation where the abnormal ends and the normal begins Thus there may be definite changes in the upper two thirds of the tibia while the lower third is normal The average rate of progress of such a lesion is about 1 cm in 2 years Radiographs reveal the shadows of arterial calcification in more than 40 per cent of cases Such calcified arteries are best seen in the lower limbs There is no evidence of a higher incidence of renal or vesical calculus in osteitis deformans than in the normal

Diagnosis —When advanced the condition is unmistakable In the early stages muscular rheumatism or osteo arthritis may be wrongly diagnosed Pulmonary osteo arthropathy is distinguished by the clubbed fingers In radiographs the amorphous type of osteitis deformans is sometimes mistaken for secondary carcinomatosis of the osteoplastic type The difference is distinct and important namely that in carcinomatosis the bones are neither enlarged nor bowed Syphilis of bones is now very rare but when only one or two bones are involved in a supposed case of Paget s disease the Wassermann reaction should be performed

Prognosis —Because the disease is uncommon there is a tendency to regard its effects as dreadful To announce the diagnosis as though it were a profound mystery may alarm both patient and relatives unnecessarily Paget s disease is slowly progressive but does not usually shorten life Thus one patient though much deformed continued to drive a crane in a dockyard 15 years after the onset of the disease Another was quite happy to have somebody hold him on a rock while he fished a stream long after he was unable to walk unaided Death usually results from the effects of arteriosclerosis or intercurrent infection and only rarely from compression paraplegia or sarcoma of bone

Treatment —No known treatment alters the course of osteitis deformans in the slightest degree *Since the bones at one stage are sufficiently decalcified to bend* methods have been used which aim at increasing the calcium intake The patient is given a high calcium diet that is a diet containing 3 pints of milk or milk products daily together with butter cheese and eggs If milk is not tolerated in these quantities calcium caseinate or calcium lactate (10 g a day) may be prescribed Vitamin D may be conveniently given in the form of tab calciferol (3000 units) one or two daily The claim that prolonged exposure to general ultra violet irradiation has resulted in increased density of the shadows of bones *in radiographs has not* been confirmed Such treatment can be carried out starting with short exposures to the mercury vapour or carbon arc lamp Paget treated his patients with potassium iodide but was not enthusiastic over the results When there is pain in the bones Lugol s solution (of iodine in potassium iodide) may be given in milk beginning with a dose of 3 minims three times a day and increasing to ten times this amount *If* iodine fails to relieve the pain aspirin or tabs codeine co *B P should be tried Exploration* of the neck for a parathyroid tumour is never justified Osteotomy is rarely necessary but it is interesting that when portions of bone have been removed for histological section relief of pain has sometimes occurred Occasionally and especially in those cases with secondary osteo arthritis of the hip joint or knee joint an ambulatory splint supporting the weight of the body on the tuber ischii is of value *A cork sole is often necessary* and when kyphosis causes pain a spinal jacket is useful

LEONTIASIS OSSEA

Synonyms —General Hyperostosis of the Skull Cranio sclerosis Megalo cephaly, Fibromatosis Osteoplastica Osseum

Definition —The term leontiasis ossea is now used in two senses specifically *for* a progressive sclerosing hyperostosis of the skull and *symptomatically* when osteitis deformans and the various types of osteitis fibrosa happen to involve the bones of the calvaria and face

Ætiology —This is unknown The fact that the disea e commonly arises in the region of the nasal sinuses has led to an erroneous view that it is infective in origin

Pathology —When Virchow suggested the use of the term leontiasis ossea in cases of hyperostosis of the skull he had in mind fibroma molluscum in which masses of new connective tissue develop in the skin He believed that the overgrowth of bone in hyperostosis corresponded exactly to elephantiasis of the soft parts and he decided to call these cases leontiasis ossea not becau e the bone disease produced a leonine appearance but because he considered it to be analogous to the disease of the soft parts which did The disease is very rare It occurs in either sex arising usually in early adult life In most instances it begins in the nasal fossæ and sinuses though in some cases the origin is near the orbit or in the base of the skull Dense ivory bone appears and spreads slowly under the periosteum being held up sometimes in the region of the suture lines but ultimately breaking through and spreading in many directions across the skull The serum calcium and plasma phosphorus are normal

Symptoms —The early clinical features include nasal obstruction blocking of the lacrimal ducts and alteration in the shape of the face and jaws Ultimately large masses of bone increasing in various directions give rise to terrible disfigurement The cavities of the mouth nose and orbit may be greatly lessened The eyeballs may protrude even beyond the lids and blindness may occur from optic atrophy There may be loss of the sense of smell and interference with the mobility of the lower jaw Except in the later stages pain is unusual

Diagnosis —Paget s disease usually begins at 55 and the pelvis spine and lower limbs are nearly always affected Generalised osteitis fibrosa leads to decalcification of the whole skeleton with a high blood calcium and low blood phosphorus Focal osteitis fibrosa often shows multiple lesions scattered throughout the skeleton

Treatment —No treatment has any permanent effect though it may be possible to remove some of the more disfiguring masses of bone

HYPERPARATHYROIDISM (GENERALISED OSTEITIS FIBROSA CYSTICA (see p 501)

FOCAL OSTEITIS FIBROSA

Synonyms —Osteitis Fibrosa Circumscripta (Schmidt) Local Fibrocystic Disease Benign Giant celled Tumour Osteoclastoma Osteogenetic Myeloma Myeloid Sarcoma

Definition —A focal or multifocal disease of bone unassociated with constitutional symptoms or with any known endocrine disturbance

Ætiology —This is unknown The disease occurs chiefly in adolescence and is much more common than is generalised osteitis fibrosa (hyperparathyroidism)

Pathology —The lesions are benign firm grey or brown tumours Histologically

they show osteogenetic fibrous tissue and giant cells which, of course are osteoclasts This explains the numerous synonyms which are used The tumours sometimes expand the corticalis and may give rise to cysts lined by osteoclasts Even when the lesions are multiple the rest of the skeleton consists of normal bone The figures for serum calcium and plasma phosphorus are invariably normal, a finding in striking contrast to that of the generalised disease The calcium balance is usually normal and, taken in conjunction with the normal blood chemistry, this finding is strong evidence against hyperparathyroidism

Symptoms —The malady affects one or more bones, is usually not disabling is of slow progress and shows a tendency to become arrested Pain is unusual and the disease is often symptomless until spontaneous fracture occurs Severe cases of the multifocal type may show considerable deformity, especially of the pelvis femora and skull

Radiographic appearances —In radiographs the principal changes are found in the ends of the long bones Usually more than one third of the shaft is affected by a fusiform enlargement composed of a pale cyst like area divided by a few coarse trabecular strands The cortex is thin and may be expanded The periosteum and adjacent bone are normal Radiographs taken with controls show that the whole skeleton apart from the lesions is normally calcified The floor of the skull and the lower jaw may be affected

Diagnosis —The normal blood chemistry serves to distinguish the focal from the generalised disease In adult cases it is sometimes difficult to differentiate between focal osteitis fibrosa and osteitis deformans and it may then be necessary to follow the progress of the condition over a period of time before a definite conclusion is reached

Treatment —Fractures are treated in the usual way If spontaneous fracture occurs in a long bone through one of the lesions union is usually strong and radiographs subsequently show that the pale cyst like area of osteitis fibrosa becomes filled with bone Exploration of the neck for a parathyroid tumour is quite unjustified

THYROTOXIC OSTEOPOROSIS (see Hyperthyroidism p 493)

OSTEOMALACIA

Synonyms —Mollities Ossium Adult Rickets

Definition —A generalised disease of the skeleton in which there is defective calcification of osteoid tissue accompanied by an insufficiency of phosphates or calcium salts in the blood The condition may arise in several ways of which three will be described In dietetic osteomalacia it is due to inadequate intake of vitamin D and calcium salts and in idiopathic steatorrhœa to impairment of absorption In the Fanconi syndrome defective tubular reabsorption of phosphates leads to their excessive loss in the urine

Ætiology —Osteomalacia is rare in England It is endemic over wide areas in Northern India Japan and Northern China and occurs sporadically in the Rhine Valley Danube Valley Vienna and certain parts of Italy Switzerland Flanders and the Balkans Heredity plays no part The disease pre eminently affects women and is likely to recur earlier and with greater severity with each successive pregnancy It is a mistake however to suppose that pregnancy is essential in the ætiology The malady is sometimes seen at puberty and is quite well known to occur though rarely in boys and men In the majority of cases the symptoms begin between the twentieth and thirtieth year

Pathology —Rickets and osteomalacia are essentially identical What difference

exists is merely that of age incidence Osteomalacia is adult rickets Morbid anatomists agree that in rickets and osteomalacia the essential abnormality is a deficient calcification of osteoid tissue This deficiency is generalised throughout the skeleton The broad osteoid seams in both diseases are due to deficiency of the calcifying mechanism which should convert osteoid tissue into true bone In osteomalacia the bones throughout the skeleton are so soft that they readily bend and cut with a knife like rotten wood Spontaneous fractures are common The blood chemistry is comparable in experimental rickets of rats in children with rickets and in women with osteomalacia The plasma phosphorus and sometimes also the serum calcium are diminished, and the serum alkaline phosphatase is raised The occurrence of fœtal rickets has been proved in babies born of osteomalacic mothers

Symptoms —Pain is a prominent symptom It occurs especially in the back and thighs is aching in character and is worse in the winter months The pelvis thorax or long bones exhibit deformity in a haphazard way one woman suffers in the pelvis another in the ribs and a third in both Besides the changes in the pelvis marked deformities occur in the chest and spine Severe kypho scoliosis may reduce the height by several inches and cause the head and neck to sink downwards and forwards on to the chest Deformities of the sternum and ribs give rise to marked prominences and depressions in the chest wall Coxa vara and irregularly curved long bones are less common The bones are soft and flexible rather than fragile so that bending is much more common than is spontaneous fracture though both are well recognised The patient develops a characteristic waddling gait and muscular weakness may add to her incapacity In many cases the pelvic deformities interfere with marital relations or with labour Cæsarean section frequently being necessary Tetany is common The teeth are normal The course of the disease may be fairly rapid lasting several months but untreated cases extend over many years The patient then becomes bedridden spontaneous fractures anæmia cachexia and bed sores adding to her discomfort and to the difficulties of nursing

Radiographic appearances —The degree of lack of calcification in radiographs will vary with the severity of the disease and it is therefore important to take radiographs with controls In the slight cases the bones of the patient will be slightly more translucent than those of the control The cortex will be less dense than normal but the bone pattern especially the trabeculation will be accentuated by contrast In the severe examples there will be little or no difference between the density of the bone and surrounding soft tissues and the cortex will appear as a mere pencilled outline The bone pattern will have disappeared the long bones will bend and occasionally show fracture All deformities apart from fracture are the result of weight stress or muscular action The pelvis is tri foliate owing to the thrusts of the heads of the femora and sacrum Lordosis is marked and kyphosis may be present In severe cases the chest and ribs are usually deformed The vertebræ are biconcave having the appearance of fish vertebræ In severe cases the vault of the skull may show numerous areas of uneven translucence varying in size and shape but all fairly clean cut The spontaneous fractures are usually subperiosteal and radiographs sometimes show pseudo fractures These appear as areas of complete translucence running across the bone the edges being quite clean cut and separated from each other by 1 or 2 mm

Diagnosis —The occurrence of pregnancy and the examination consequent upon this lead commonly to the recognition of the pelvic deformity and of the disease which has given rise to it Differential diagnosis from other generalised diseases of the skeleton usually produces no difficulty In hyperparathyroidism there is a high serum calcium a low plasma phosphorus and an increased calcium excretion in the urine In senile osteoporosis the patient suffers from kyphosis and a tendency to fractures particularly of the neck of the femur and the blood chemistry is normal In thyrotoxic osteoporosis the usual signs of hyperthyroidism are present and the

blood chemistry is normal In multiple myeloma the Bence Jones protein is found in the urine in 75 per cent of cases the serum globulin is usually increased and the albumin globulin ration diminished The serum calcium is usually normal but sometimes raised The plasma phosphorus is normal but it rises in cases showing renal insufficiency In radiographs the condition may closely resemble osteomalacia

Treatment —Pure vitamin D is called calciferol because of its power to induce calcification in tissues especially in osteoid tissue It is 300 000 times as potent as cod liver oil weight for weight The good effects not only of calciferol but also of cod liver oil and ultra violet irradiation have been noted both clinically and chemically, since they are capable of raising the serum calcium to normal In cases where tetany is present calcium salts should be administered in addition The diet of a woman suffering from osteomalacia should contain 3 pints of milk a day with plenty of milk puddings, eggs, butter, cheese, green vegetables and even nuts and raisins The dose of cod liver oil should be large up to 2 or 4 oz daily This treatment relieves the pain in 3 to 4 weeks Some cases are refractory and it is then necessary to add 0 5 mg of calciferol to the cod liver oil daily Tetany is rapidly removed by treat ment with cod liver oil and calcium lactate A powder containing at least 10 gm of the latter should be used daily and is best administered fasting with a glass of milk The patient should be exposed to sunlight when this is possible, otherwise treatment by ultra violet irradiation may be used starting with a short exposure to a carbon arc lamp and increasing gradually up to 30 minutes There is no evidence that phosphorus is of any value in the treatment of osteomalacia Where the disease exists in great endemic areas questions of diet and social and religious customs are proving very difficult In large areas of China and India the diet is often deficient in quantity and inadequate in calcium and vitamin D In the high mountain valleys of these countries and in areas of India where purdah is practised darkness adds to the danger by causing further deprivation of vitamin D With regard to China Maxwell states ' We want flocks and herds milk and meat with security of life and property The suggestion has been made that it might be practicable in India and China to dispense calciferol freely at a low price just as quinine is dispensed in malarial districts The relation of ovarian function to calcium metabolism has not yet been settled Osteomalacia gets worse during lactation no doubt because of the great drain of calcium from the body Improvement has been observed after ovariec tomy This operation may act merely by preventing pregnancy and it is presumably just as reasonable to ligate the Fallopian tubes The pelvic deformity may necessitate Cæsarean section

OSTEOMALACIA IN IDIOPATHIC STEATORRHŒA

When osteomalacia occurs in the course of idiopathic steatorrhœa (Gee s disease) the following features may be present fatty stools dilatation of the colon tetany, anæmia skin lesions and infantilism (see p 620) The disease occurs in both sexes and the history nearly always goes back to early childhood The symptoms develop in spite of an adequate diet We must therefore suppose that there is some disturb ance of gastro intestinal function resulting in deficient production absorption or utilisation of one or more essential factors The serum calcium is low and the plasma phosphorus is low or normal The total fat in the stools may reach 40 per cent or more and the bulk of this is unsplit fat The clinical and radiological features are exactly the same as in dietetic osteomalacia An opaque enema will reveal dilatation of the colon In treatment the fat in the diet must be cut down to a minimum and the calcium salts and vitamins kept high Vitamin D must be given in a solid and not in an oily medium The prognosis of this type of osteomalacia is good especially in young people Splinting or even osteotomy may be necessary to correct deformities such as genu valgum The pelvic deformity may necessitate Cæsarean section

THE FANCONI SYNDROME

Synonyms—The de Toni Fanconi Syndrome Hypophosphatæmic Rickets with Renal Glycosuria Osteomalacia with Renal Glycosuria

Definition—A rare form of osteomalacia readily identified by the presence of renal glycosuria and persistent amino aciduria The bone changes are due to excessive renal excretion of phosphates

Ætiology and Pathology—There is impaired tubular reabsorption of glucose amino acids bicarbonate and phosphate probably due to an inborn error of enzyme metabolism It was first described in children by Fanconi in 1931 and was identified in adults and found to be hereditary in 1935 In some cases storage of cystine in the reticulo endothelial system has been found at necropsy Although the association of inhibition of growth and rickets with cystinosis has been known since the work of Lignac in 1924 the relationship between disturbances of cystine metabolism and the Fanconi syndrome is still imperfectly understood The following amino acids have been identified in the urine in abnormally large amounts aspartic acid glutamic acid glycine serine alanine threonine valine cystine leucine tyrosine arginine hydroxyproline and phenylalanine The excessive drain of phosphates through the kidneys leads to a constant low level of inorganic phosphate in the blood which may reach a figure of less than 1 0 mg per 100 ml As a result of this the ossification of osteoid tissue in the skeleton is always imperfect

Symptoms—The disorder is usually discovered in infancy even in babies of 2 months Sometimes it does not make itself evident until adult life In children the skeletal changes of rickets appear and there may be dwarfism and infantilism Loss of appetite polydipsia and polyuria are commonly present The urine shows marked increase of ammonia glucose from time to time and albumin rarely a variety of amino acids can be identified by chromatographic methods (see above)

Radiographic appearances—Radiographs of the bones cannot be distinguished from those of ordinary rickets The changes include absence of calcification of the metaphyses with saucer like splaying of the growing ends of the bones extreme poverty of calcification of the cortex and spongiosa deformities fractures and poorly calcified callus Where infantilism is present the state of development of the bones of the carpus is correspondingly delayed In adults the spine shows well marked osteoporosis individual vertebral bodies being bi concave In radio graphs the pelvis the long bones and especially the bones of the hands and feet are very poorly calcified The ivory corticalis is either reduced to a mere shell or it retains its normal thickness and is greatly reduced in density The spongiosa is deficient owing to disappearance of the smaller spicules and in some places only the coarser trabeculæ are left Fractures and deformities are constant Bowing of the humerus radius and ulna is common and bowing and twisting of the femur is found in many cases Subperiosteal fractures unsuspected by the patient are seen in radiographs in every case The pelvis is usually trifoliate owing to the thrust of the femora and in advanced cases the deformity is grotesque The extreme poverty of calcification ometimes progresses to such a degree that it is difficult in radio graphs to distinguish between bone and soft tissue Nevertheless the skull is often little affected and usually shows only a fine mottled appearance

Prognosis—Fractures of bones recur and may be multiple Extreme deformity of the thoracic cage usually ends in death from broncho pneumonia Though damage to the liver is not an invariable feature of the Fanconi syndrome focal necrosi fibrosis and even primary carcinoma of the liver do sometimes occur even in children Rarely the renal lesion progresses in such a way as to cause nitrogen retention and consequent death

Treatment —The osteomalacia responds imperfectly to vitamin D in large doses A moulded steel spinal support or other orthopædic apparatus may be needed When *there is acidosis due to loss of bicarbonate in the urine* sodium bicarbonate or citrate should be administered by mouth Portal obstruction and hepatic or renal insufficiency will need symptomatic treatment

OSTEOGENESIS IMPERFECTA

Synonyms —Fragilitas Ossium Congenita, Osteoporosis Congenita, Congenital Osteopsathyrosis Osteopsathyrosis Idiopathica

Definition —*A* generalised disease of the skeleton in which the bones are so fragile that repeated fractures occur Multiple fractures may occur *in utero* (pre natal type of Vrolik 1849) or fractures may not occur until after birth (post natal type of Lobstein 1833) The disease is congenital and in some 25 per cent of cases *hereditary Both sexes are affected equally*

Ætiology —This is unknown

Pathology —In both types the basic defect appears to be defective osteoblastic activity The cortex of the bones may be *scarcely thicker than paper* and the trabeculæ of spongy bone are extremely thin In the pre natal type many fractures are seen in some cases practically every bone in the body has been fractured The older fractures exhibit good callus formation In extreme cases especially in the pre natal type, the cranial ossification is so disorganised that the vault of the skull consists of a mosaic of small Wormian bones Congenital hypoplasia occurs in other mesen chymal tissues notably the ligaments and the sclerotics There is no evidence what *ever of vitamin deficiency No* abnormality in the serum calcium, plasma *phosphorus* or calcium output has been demonstrated The plasma phosphatase tends to show a raised value but this is not constant

Symptoms —The *general* health of the patient is good but fractures occur from the most trivial violence or even normal muscle action In the course of time 20, 30 or even 100 spontaneous fractures may occur They are often subperiosteal and cause little pain The patient tends to be short in stature and slender in build As a result of anomalous cranial ossification the shape of the head is often striking A bitemporal protuberance so marked as to turn the ears outwards is frequently observed but protuberances in the occipital and frontal regions are also seen Every bone in *the body may be deformed The limbs are often bowed and of unequal* length Kypho scoliosis distortion of the ribs and sternum and asymmetry of the pelvis all occur Three other defects are commonly found in association with the fragile bones namely leaden blue sclerotics a tendency to dislocation of joints and after the age of 20 years otosclerotic deafness Amongst the adult population affected with blue sclerotics approximately *60 per cent* have an associated *liability to fracture,* approximately 60 per cent an associated otosclerosis and 44 per cent suffer from all three defects Osteogenesis imperfecta sometimes occurs *in an hereditary* form without blue sclerotics

Diagnosis —Severe cases and all those with blue sclerotics are unmistakable In the new born *great* shortening of the limbs may suggest achondroplasia but the skull is quite different Cases of spontaneous fracture in the adult occurring in hyperparathyroidism hyperthyroidism myelomatosis osteoclastic carcinomatosis and neuropathic atrophy of bones really cause no difficulty

Prognosis —Severe cases of the pre natal type are either stillborn *or live only* for a short time In post natal cases the condition proves more severe the earlier the first fracture appears Multiple fractures in the first few years of life may lead to such deformities *that the patient can never* walk and may die before puberty In those who survive the liability to fractures tends to become less before puberty

In general the longer the patient lives the greater will be the improvement, and in many of the adult cases the disability is slight only

Treatment —The utmost care must be taken to avoid the occurrence of fractures Treatment consists in gentle handling and careful splinting Union usually occurs without delay and is firm Dislocations are reduced without difficulty Vitamin D calcium salts and a high calcium diet have no effect on the course of the illness

OXYCEPHALY

Synonyms —Tower Skull, Steeple Head, Sugar Loaf Head Acrocephaly Craniostenosis

Definition —A congenital deformity of the skull due to premature synostosis of the cranial sutures The skull is short from front to back and its vertical diameter is increased Allied forms of craniostenosis are scaphocephaly the boat shaped head and plagiocephaly the obliquely flattened head

Ætiology —This is unknown The disease is more common in males than females It is sometimes hereditary and familial It is usually present at birth but it may develop subsequently up to the age of 6

Symptoms —In its slightest form it attracts attention while in its grosser forms there is no passer by but is shocked by the disfigurement and repelled by its hideous ness The forehead is much increased in height sloping gradually upwards to the vertex with feebly marked superciliary arches The vertex of the skull appears pointed instead of flattened or rounded and a thin bony prominence is sometimes felt in the region of the bregma The hairy scalp may be raised above the normal level and present the appearance of being perched on the top of a cone Viewed laterally the ears appear placed on a lower level than normal Proptosis is present in most cases and it may be so considerable that the eyeballs become dislocated in front of the lids Failure of closure of the eyes especially during sleep may lead to lacrimation and conjunctivitis Divergent squint is common and nystagmus is present in some cases Symptoms arise from insufficient room within the skull for the developing brain There is increased intracranial pressure with headache and sometimes vertigo The condition is compatible with normal intelligence but not infrequently optic atrophy supervenes This is secondary to papillœdema in some 85 per cent of cases In the remainder it is brought about by narrowing of the optic foramen and is of the primary type The sense of smell is often completely lost but taste is affected very rarely Hearing is unaffected The following associated congenital malformations have been described in a few cases webbing of the fingers and toes malformation of ears elbow and shoulder joints and fingers

Radiographic appearances —Radiographs show an increased vertical diameter of the skull with its highest point either at the bregma or somewhere between it and the lambda The anterior fontanelle closes late and its site is marked by a slight protuberance over which the bone is thinned The sutures of the vault are partly or entirely absent but the basal suture between the sphenoid and the occipital bone may be widely open The air sinuses are rudimentary and the middle fossa bulges forward The most characteristic feature is the presence of numerous deep con volutional markings

Prognosis —The optic atrophy whether primary or secondary may advance to complete blindness There is nothing to show that oxycephaly shortens life

Treatment —Anodynes should be used in the relief of headache If the symp toms of increased intracranial pressure become marked and the changes in the optic discs progress decompression may be necessary

DISEASES OF ENDOCHONDRAL OSSIFICATION

ACHONDROPLASIA

Synonyms —Chondrodystrophia fœtalis (Kaufmann), Micromelia fœtalis

Definition —A disease of fœtal life in which defective endochondral ossification makes the bones preformed in cartilage short, but stout and strong

Ætiology —This is unknown Both sexes are affected equally It is hereditary and has been recorded in six generations Several members of the same family may be affected *The condition is unrelated to rickets cretinism syphilis or tuberculosis*

Pathology —The essential abnormality is found in the cartilaginous epiphyses The cartilage does not prepare itself for ossification, which is in consequence so slow that the long bones are too short Since however the periosteum goes on laying down bone normally the bones are stout and strong The membrane bones of the skull are unaffected, so that the calvaria is of normal size Premature synostosis of the cartilaginous bones at the base of the skull leads to shortening and consequent depression of the bridge of the nose The clavicles are not affected The pelvis is distorted and contracted *the sacrum being tilted forwards Extreme lordosis may* be present The costo chondral junctions are enlarged to form a rosary The scapula is so small that the glenoid fossa scarcely holds the head of the humerus

Symptoms —The patient is dwarfed but of normal intelligence The usual height of the adult is about 4 ft The vault of the head is large and the frontal and parietal eminences prominent The face is small and the nose has a depressed and flattened bridge The nostrils are large the lips thick and the lower jaw and chin well developed The teeth are normal The trunk is of normal size but the extremities are much shortened and with the arms at the sides the fingers reach no farther than the great trochanter of the femur The humerus and femur are relatively more shortened than the other bones of the extremities so that the proximal segments of *the limbs show the most marked shortening The arms are muscular and* are held a little abducted from the trunk The hands are short thick and trident shaped the fingers being almost equal in length The lower limbs are thick and often show deep transverse furrows as if there were redundancy of the soft parts This appearance is due to the packing of well developed muscles into the restricted long axis of the limb This muscular development enables the achondroplasic to perform feats which are surprising in one so small He rises from the lying down position by a characteristic springing movement from the legs without any assistance from the arms The curving and enlargement of the ends of certain bones gives rise to bow legs and beading of the ribs The lumbar curve is increased owing to tilting forward of the sacrum and excessive development of the buttocks In consequence the gait has a peculiar *duck like waddling character The genital organs are normal* The fact that the female may become pregnant makes the pelvic deformity of great importance The conjugate diameter is greatly narrowed and it is almost impossible for an achondroplasic woman to give birth to a living child except by Cæsarean section That the disease has existed for something like 5000 years is known from models found in mummies of two achondroplasic gods of ancient Egypt namely Ptah Sokar and Bes In the Middle Ages the attractive antics of achondroplasics made them much sought after as court jesters or dwarfs To day not infrequently they play the parts of clowns at fairs circuses and music halls and sometimes break chains on the stage

Diagnosis —In the new born the great shortening of the limbs may suggest osteogenesis imperfecta but the skull is quite different In childhood the malady is readily distinguished from rickets and congenital syphilis by careful attention to the physical signs Achondroplasia differs from cretinism in that the patient is of

average intelligence and has normal skin hair and voice The pituitary dwarf presents no difficulty because the limbs and trunk are in perfect proportion

Prognosis —The majority of infants suffering from achondroplasia are either still born or die shortly after birth If the child does survive the expectation of life is normal The female achondroplasic faces greater risks in parturition than a normal woman

Treatment —No treatment is of any avail Orthopædic treatment for bow legs is unnecessary The pelvic deformity may necessitate Cæsarean section

DYSCHONDROPLASIA

Three clinical conditions are included under this heading In all of them islands of ectopic cartilage are found giving rise to multiple ecchondromata or enchondromata The three conditions are grouped together because of one feature they have in common namely arrest or perversion of the normal process of endochondral ossification in certain bones This change differs from that seen in achondroplasia only because it is neither symmetrical nor universal Different manifestations of dyschondroplasia may occur in various members of the same family

(i) *Hereditary multiple ossifying ecchondromata* (*hereditary deforming chondrodysplasia diaphysial aclasis or multiple exostoses*) This is a fairly common disease in which multiple bony tumours are found in association with certain other skeletal deformities It is hereditary and may affect several individuals of the same family It is more common in males than in females in the proportion of 3 to 1 It is usually discovered in childhood Palpable bony tumours up to 2 cm or more across are found more or less symmetrically placed near the knee shoulder hip ankle and wrist The scapula ribs and pelvic bones may sometimes be affected The stature is shortened and the limbs may be unequal in length In the majority of cases the ulna and fibula are disproportionately short in relation to the radius and tibia Bowing of the radius ulnar deviation of the hand irregular length of the fingers and valgus deformity of the foot all may occur Sarcoma supervenes in 5 per cent of cases Local exacerbation of symptoms in a patient over 30 years of age may be the first indication of its onset Rarely pressure of an exostosis upon the spinal cord may cause paraplegia or upon a nerve trunk pain or local paralysis Aneurysm has been recorded from pressure upon an artery The radiological appearances are characteristic The metaphysis of the bone affected is broadened and distorted and ossifying ecchondromata with broad bases and pointed tips project from it The cartilaginous cap of the tumour is not seen unless it is calcified The earlier the ecchondroma occurs the nearer to the centre of the shaft will it be Where ecchondromata protrude between adjacent bones such as the tibia and fibula local fusion may occur The ulna is likely to be short and to end in a point articulating with the radius on its mesial aspect but not partaking in the carpal articulation Usually no treatment is required but should it be necessary to remove any particular swelling this is easily carried out.

(ii) *Multiple chondromata* (*Enchondromatosis*) This is a rare disease affecting the bones of the hands and feet Cartilaginous swellings in the fingers and toes begin in childhood and increase in size up to the age of 30 years The swellings are firm elastic rounded and slightly translucent The skin over the larger ones may be tightly stretched and shiny and show prominent veins The hands and feet may become hideously deformed Sometimes a rib near the costal cartilage the sternum the pelvis and the scapula are affected In certain cases the ulna and fibula are disproportionately short as in diaphysial aclasis Spontaneous fractures may occur and sarcoma may supervene after years Radiologically chondromata are seen as rounded eccentric, translucent areas expanding the corticalis interrupting its outline and projecting into the soft tissues Sometimes the swellings are trabeculated and they may

contain dense punctate calcified areas Where operation is undertaken to excise some of the chondromata care must be exercised to avoid spontaneous fracture of the phalanges or metacarpals

(iii) *Unilateral chondrodysplasia (Ollier's disease)* This is a very rare type of chondrodysplasia occurring in children and sometimes familial It usually has a completely unilateral distribution but some cases have only one bone or one limb affected, and others are bilateral *Some abnormality is often first noticed between* the first and second years of life when as a rule, one limb is found to be shorter *than its fellow* The difference in length becomes progressively greater as growth proceeds Deformity may occur either because weight bearing causes bending of the bone or because of the different rate of growth where only one of the paired bones is affected Most patients seem to reach adult life when their symptoms are mainly those of their deformities and sometimes of a secondary arthritis In a small proportion of cases sarcoma supervenes *The diagnosis largely depends* upon examination of radiographs The ends of the long bones show translucent longitudinal striæ interrupted by small pale mottled areas and dark punctate spots *In the areas* affected there is extensive alteration in the pattern of the corticalis and spongiosa but the centre of the shaft remains normal As the child grows older the typical striped appearance disappears and is replaced by dense punctate speckling due to areas of calcification The disease has occasionally been mistaken for osteitis fibrosa but the radiological appearances are pathognomonic Treatment is concerned with the prevention and relief of deformities and proceeds along the usual orthopædic lines *Osteotomy is sometimes necessary Fractures are of fairly common occurrence,* and like the osteotomies appear to unite well

DISEASES OF THE BONE MARROW

MULTIPLE MYELOMA

Synonyms—Myelomatosis Kahler's Disease Plasmacytoma *Hæmatogenous* Myeloma

Definition—A fatal disease characterised by the development of multiple tumours in the skeleton, which arise from cells of the bone marrow It is very rare The bones are affected in the following order of frequency spine ribs, sternum skull scapula pelvis, clavicle humerus and femur

Ætiology—Multiple myeloma is of unknown origin It is a malignant neoplasm of the hæmatogenous marrow occurring *in multiple foci* The disease is related to leukæmia but differs from it in the sharper localisation of the neoplasia the absence of enlargement of the spleen or lymph glands the much smaller tendency for the abnormal cells to enter the blood stream and the frequent appearance of Bence Jones protein in the urine Intermediate forms occur with features of both diseases It is associated with interesting alterations of protein metabolism The disease is sometimes familial It begins typically at the age of 55 and only 10 per cent of cases occur before 40 The sexes are affected in the proportion of 3 men to 2 women

Pathology—Multiple deep red or reddish grey sharply defined tumours are found distributed *throughout the red bone marrow* They are usually a few millimetres in diameter and very numerous Occasionally a tumour may reach a diameter as great as 5 cm They are composed of blood forming cells which resemble plasma cells They erode bone sometimes expand the cortex and cause deformities and spontaneous fractures Rarely a diffuse hyperplasia of the marrow is associated with foci of tumour formation Tumours may also be found outside the skeleton in the tonsils, liver spleen kidneys or sex glands and these *lesions may even precede those*

in the bones The marrow tumours give rise in the urine to the Bence Jones protein which appears as a cloud when the urine is heated to 55 C redissolves at 85 but reappear on cooling It is found in 75 per cent of cases from a trace to a large amount In some cases it appears early in the disease in others late Its occurrence may be continuous or periodic Sometimes a substance allied to amyloid material is deposited in the muscles and in nodules connected with the periosteum bursæ tendon sheaths and joints It is possible that both the Bence Jones protein and the amyloid substance are produced from the breakdown of myelomata The serum globulin is usually increased even as much as to 8 per cent (normal 2 per cent) The albumin globulin ratio may drop from the normal 2 2 to a figure as low as 0 5 The formol gel reaction is positive (see p 267) and there is a very rapid rate of sedimentation of the blood Metastatic calcification while by no means constant has been frequently observed in the kidney lung stomach myocardium and uterine mucosa The serum calcium is usually normal but taking into account the bone destruction which occurs as the result of erosion by the marrow tumours and also the metastatic calcification it is not surprising that high serum calcium values have sometimes been recorded Figures from 13 to 16 mg per 100 ml have been found Those cases with a normal serum calcium have a normal calcium output while those with a high serum calcium have an output up to double the normal Where renal insufficiency complicates multiple myeloma the plasma phosphorus is found to be high and may rise as the kidney condition becomes worse The parathyroids are not enlarged in multiple myeloma

Symptoms —The initial symptom is pain often bilateral in the thoracic abdominal and lumbar regions and sometimes in the neighbourhood of the joints Progressive kyphosis or angular curvature of the spine with loss of total height follows The spine sternum and ribs may be tender on percussion It is unusual for any of the myelomata to be palpable In 60 per cent of all cases spontaneous fracture occurs in the ribs sternum or later in the long bones In no other type of bone tumour does pathological fracture occur so frequently In some cases amyloid masses may be palpable as firm rounded slightly tender subcutaneous nodules more than a centimetre in diameter They are felt especially in the scalp along the spine near the joints and in the musculature particularly that of the pelvic and shoulder girdles There is usually a hypochromic anæmia which becomes aggravated in the terminal stages In a few instances cells of the type which constitutes the tumour enter the blood stream in larger or smaller numbers and it is probable that they can be found in the majority of cases if a sufficiently careful search is made In rare instances the anæmia is of the leuco erythroblastic type Nephritis without hypertension is fairly common The temperature is usually normal but recurring fever has been observed The patient ultimately becomes bedridden and cachectic It seems justifiable on clinical grounds to consider separately what may be called the vertebral form of the disease Here the growth is confined for some time to the vertebral and extradural tissues Moreover death may occur before the growths become widespread and sometimes without the Bence Jones protein having appeared in the urine In this variety the patient rapidly develops signs of a transverse spinal lesion with blockage of the spinal canal The thoracic cord is usually the site of compression and there is focal spinal tenderness Radiographs show destruction of the corresponding vertebral body

Radiographic appearances —In radiographs the marrow tumours are found mainly in the spine ribs sternum and skull They are seen as clean cut elliptical or circular areas of complete translucence set closely together and varying from 1 mm to 5 cm in diameter The large tumours may expand the cortex of the bone affected There is a good deal of generalised osteoporosis throughout the affected bones The spine shows collapse of the bodies of one or more vertebræ The skull is not thickened Spontaneous fractures especially in the ribs are very common

Diagnosis—Once the lesions have appeared in many bones the diagnosis is easily made The age of the patient, multiple involvement of the bones of the thoracic cage spontaneous fracture of a rib Bence Jones protein in the urine progressive anæmia, cachexia and characteristic radiographs make an unmistakable clinical picture Biopsy of a portion of bone or examination of a bone marrow smear from a sternal puncture may reveal the characteristic myeloma cells Secondary carcinomatosis of bones may cause difficulty, especially in cases in which the primary growth is symptom less It is essential to differentiate the disease from generalised osteitis fibrosa (hyper parathyroidism) There is some resemblance in the clinical picture as it affects the skeleton but the presence of the Bence Jones protein and the blood chemistry are characteristic In multiple myeloma the serum calcium is usually normal If it is high it is associated with a high plasma phosphorus, whereas the characteristic effect produced by parathyroid hyperfunction is a high serum calcium with a low plasma phosphorus In osteomalacia the patient is usually a woman in the child bearing period of life, and a good deal of bending occurs in the bones The blood chemistry is characteristic Sometimes in the early stages of multiple myeloma widespread pain in the thoracic abdominal and lumbar regions may lead to a mistaken diagnosis of fibrositis In tuberculous caries of the spine neither the ribs nor the sternum are involved The fact that the Bence Jones protein is found in the urine in an occasional case of leukæmia need cause no mistake In those cases in which nephritis complicates multiple myeloma the albuminuria may cause difficulty The Bence Jones protein may be detected in the presence of albumin by making the urine slightly acid with acetic acid boiling it and filtering while hot using a funnel with a hot water jacket If Bence Jones protein is present the filtrate will become cloudy as it cools

Prognosis—The prognosis is hopeless Death often occurs within 6 months of the onset of symptoms but occasionally a patient survives for 2 years or more Broncho pneumonia cachexia or compression paraplegia with ascending pyelo nephritis are the usual terminal events

Treatment—The patient should be treated by rest in bed, anodynes and suitable splinting when necessary Occasionally deep X irradiation can be used with good effect It alleviates pain and reduces the size of the tumours but it does not retard the progress of the disease It is clearly unjustifiable to explore the neck in search of a parathyroid tumour When the symptoms and signs point to compression of the spinal cord surgical intervention may be worth while Laminectomy reveals a grey or reddish grey extradural mass either pushing the cord backward or encircling it Removal of the mass decompresses the cord and is followed by improvement Deep X irradiation and the wearing of a spinal brace are advised after laminectomy

GAUCHER S DISEASE

In 1922 Pick discovered a gross osseous form of Gaucher s disease It is exceedingly rare The symptoms are pain in the bones spontaneous fractures and some times angular deformity of the spine Limitation of movement of the hip joint is sometimes found In radiographs the bones show patchy osteoporosis A character istic feature is that the lower ends of the femora are widened evenly Both skull and pelvis may be involved Sometimes scattered through the bones there are focal pale rounded areas which expand the cortex These areas are deposits of kerasin, a galactolipin The usual characteristics of Gaucher s disease are of course present (see p 784)

HAND SCHÜLLER CHRISTIAN S DISEASE

The lesions of Hand Schuller-Christian s syndrome (lipoid granulomatosis or xanthomatosis of bones) are not confined to the calvaria the orbit or the sella turcica

(see p 783) Erosions of the maxilla and mandible have been described resulting in loosening or falling out of the teeth Erosion of the petrous bones may lead to a syndrome simulating otitis media and bilateral deafness has been observed Large areas of rarefaction have been described in the long bones of the extremities and in the spine pelvis ribs and clavicles Pain may occur in the bones affected especially the head pelvis and thigh Spontaneous fracture is not uncommon When the pelvis is involved there may be deformity including shortening of one lower limb In some cases the skull escapes entirely diabetes insipidus and exophthalmos being absent Radiologically the deposits of cholesterol ester are seen as irregular clean-cut translucent areas sometimes with a few coarse trabeculæ In order to distinguish the condition from multifocal osteitis fibrosa it may be necessary to excise a portion of bone for histological section The lesions tend to yield temporarily to treatment by X irradiation

DONALD HUNTER

SECTION XVII

DISEASES OF THE SKIN

INTRODUCTION

SKIN diseases are essentially similar in their pathology to diseases of other organs or tissues Congenital anomalies acquired inflammatory degenerative and neoplastic processes affect the skin but the skin is peculiar in that it is exposed to changes of environmental conditions to physical and chemical traumata and to invasion by many different organisms Skin diseases are under the patient s direct observation to a greater extent than occurs with any other organ the lesions are often scratched and rubbed with the result that secondary changes of infection and thickening may be superimposed Self treatment and over treatment with topical applications often have unfortunate results and may mask the original pathological process Many so called skin diseases are in fact physiological reactions which have become fixed or which are excessive and too easily induced, others are pathological modes of reaction of the skin to different stresses

It is assumed that the reader is conversant with the anatomy histology and physiology of the skin and with the descriptive terms used in dermatology A few remarks about the functions of the skin are however relevant to the subsequent discussion of cutaneous pathology

The skin protects the organism as a whole from any harmful environment The epidermis acts as a tough outer covering protecting the layers beneath from excessive insolation, minor traumata and infection the sebum lubricates the horny layer and has bactericidal properties by virtue of its fatty acid content the sweat helps to keep the body temperature steady and emulsifies the sebum and helps to spread it over the body surface If the epidermal barrier against infection is breached the mesenchymal defensive mechanisms come into play with dermal and hypodermal vascular dilatation and the passage of leucocytes and tissue cells into the infected area The cutaneous blood vessels conserve body heat by contracting and dissipate it by relaxing so acting a a thermostat they al o help to keep the blood pressure steady The dermal collagenous and elastic fibres give the skin its tough yet elastic character and enable it at least in youth to conform to the underlying tissues

The sensory end organs in the skin provide for accurate localisation of touch and a delicate perception of slight variations in temperature these set into play a chain of involuntary reflexes and voluntary actions

The skin is an organ of antibody formation a fact made use of in the Mantoux Dick Schick and other tests it is also the organ of vitamin D synthesis from solar irradiation of sterols in the upper layers of the dermis It functions of excretion and of respiration are minimal and need not be considered but its power of absorption is most important some drugs and other chemicals can have serious or even lethal effects by this route

Two other functions of the skin are important to the practising physician In all communities primitive or civilised the skin is the chief organ of display some cosmetics particularly those of a synthetic nature used in civilised communities may cause inflammatory reactions in a few individuals The skin is also the chief organ of emotional expression various feelings being portrayed by alterations in tone of the cutaneous blood vessels in the amount of sweating hair erection etc, with secondary effects on the sebum epidermis and dermis

THE DIAGNOSTIC APPROACH —Bearing the above facts in mind it will be appreciated that the approach to dermatological problems has to be somewhat different from that of internal medicine The ætiology of many skin diseases and reactions remains obscure often several ætiological factors operate together or in sequence Variations of individual reaction to a particular agent for example a drug are marked on the other hand various physical chemical emotional malnutritional and infective noxæ may in the one individual produce eruptions closely similar to each other

In the sections that follow skin diseases have been grouped according to their causes when these are known when the cause is vague or unknown they have been grouped according to the presenting symptom or sign this being the most practical way of considering the differential diagnosis just as it was in the days of Robert Willan

It is essential first to obtain certain historical data in every case Only the patient knows the duration site of onset original appearance and the manner of spread of the malady whether there have been previous attacks and what the past treatments have been with their effects It is legitimate to ask the patient what he believes to be the cause when an irritant contact is suspected The patient is now examined in routine head to foot fashion unless the condition is obviously local and further questioning depends to some extent on the nature and distribution of the lesions Suitable subheadings to the history include family history past history general health personal history domestic and occupational history special attention is directed to racial characteristics and to the presence or absence of evidence of emotional instability

On inspecting the skin it is necessary to decide the nature of the eruption erythematous macular squamous papular vesicular bullous or some combination of these granulomatous nodular or ulcerative hyperpigmented or depigmented and so on This should enable the diagnosis to be narrowed down to a few possibilities The final diagnosis is then attempted from a consideration of the colour morphology and anatomical situation in the skin of any elementary lesion that may be found and from the grouping and distribution of the eruption as a whole and the presence of secondary changes if any Most dermatoses can be diagnosed on clinical evidence alone without the necessity for any pathological tests or biopsies These tests should only be used as ancillary aids in diagnosis prognosis and treatment

SENSORY DISORDERS

Excessive sensibility (hyperæsthesia) without obvious skin changes occurs in some disorders of the nervous system (*q v*) It also occurs in certain skin tumours especially glomus hæmangioma and leiomyoma and in certain inflammatory conditions for example periarteritis nodosa

Lack of sensibility (anæsthesia) is found with certain diseases affecting the nervous system particularly syringomyelia leprosy tabes dorsalis peripheral neuritis and hysteria

In syringomyelia there may be anæsthesia with trophic changes in the skin of the fingers (Morvan s disease) The shiny anidrotic skin is liable to become infected leading to destructive changes The discrimination between heat and cold is lost and the sensation of touch diminished or lost. Burns may easily occur

In leprosy depigmented or lupoid anidrotic anæsthetic or paræsthetic areas of skin may be found loss of touch heat and cold being the earliest sensory changes

In tabes dorsalis perforating ulcers of the foot are the commonest manifestations of the sensory disturbance

In diabetes and other forms of peripheral neuritis glossy skin and perforating ulcers may occur sometimes complicated by arteriosclerotic ischæmic effects

In hysteria glove and stocking anæsthesia is a common symptom and the presence of Charcot s triad of palatal anæsthesia, conjunctival anæsthesia and suggestion anæsthesia is strong circumstantial evidence suggesting that a dermatosis is being hysterically produced or maintained

Abnormal sensibility (paræsthesia) occurs in a large number of skin diseases as itching (pruritus)

PRURITUS

This term is used to describe general or local itching of the skin in which there is either no obvious local cause or physical sign or in which such physical signs as exist are secondary and due to rubbing (lichen simplex) scratching excoriation, infection or over treatment

GENERAL PRURITUS

Ætiology and Pathology —Generalised itching more commonly occurs in the elderly and is thought to be due to arteriosclerotic changes in the central nervous system There may be some atrophy of the skin but this is often seen without pruritus and it probably has no connection with the symptom

Histologically no changes are observed in the skin except possibly some degree of coincidental atrophy and the effects of physical damage

Clinical Picture —The patient complains of itching and tingling of the skin, particularly when getting dressed or undressed or a few minutes after getting into bed Hot baths or proximity to a fire aggravate the condition Loss of sleep increases the sense of irritability and helps to establish a vicious circle There may be no physical signs even when the patient complains bitterly of the distress and loss of sleep or there may be scratch marks, excoriations and areas of lichenification eczematisation and even some degree of infection

Course and Prognosis —In the idiopathic senile variety the prognosis as regards cure is poor, though longevity is not affected In all other varieties the prognosis depends on the cause

Diagnosis —General pruritus may be a symptom of diabetes jaundice uræmia or gout of intoxication by cocaine or opiates including codeine, of leukæmia or Hodgkin s disease of cutaneous reticulosis or carcinomatosis Pediculosis and scabies must be excluded itching around the shoulders may be due to *pediculosis capitis* or *corporis*, the underclothes should always be inspected for lice and nits particularly at the seams louse infestation is more often secondarily infected than is idiopathic pruritus The patient must be questioned as to the occurrence of whealing there may be none at the time of examination or dermographism may be demonstrable General pruritus may be of emotional origin especially when there is frustration or deprivation of affection If there are excoriated papules the diagnosis of dermatitis herpetiformis must be considered

Treatment —The patient if retired should be kept fully occupied so as to distract attention from the skin as much as possible Sudden changes of temperature must be avoided Baths should be pleasantly warm not hot and 4 oz of bicarbonate of soda may be added to a 25 gallon bath to relieve itching Woollen underclothing should not be worn in direct contact with the skin Condiments strong hot tea and coffee and over indulgence in alcohol must also be proscribed Sedatives such as phenobarbitone promethazine hydrochloride or butobarbitone are useful, and in milder cases a bromide and valerian mixture Opiates should not be given

For local treatment if the skin is dry hydrous ointment is useful or equal parts of glycerine of starch and lanolin In other patients a lead and calamine lotion or a

lead and glycerin lotion can be used but tar phenol menthol antihistamines and benzocaine derivatives are best avoided

LOCALISED PRURITUS

This may occur without physical signs or friction may produce the condition known as lichen simplex (*q v*) This is of variable appearance according to its situation The commonest sites are the scalp the back and sides of the neck the eyelids brows or perioral region behind and above the ears the elbows wrists or palms the external genitalia the medial aspects of the thighs the lower parts of the calves and the feet

ANOGENITAL PRURITUS

This may occur as pruritus ani in either sex as scrotal and perineal pruritus in the male, or as vulvar pruritus or combined anal and vulvar pruritus in the female

PRURITUS ANI

Pruritus ani is often present without physical signs if any signs are present they may be either the cause or the effect of the symptom

Ætiology—Often the itching starts from some transitory cause but continues after this has been removed in part owing to a vicious circle of scratching and further itching and in part owing to the relief of emotional tension that seems to be provided in some individuals from this practice Anal irritation may be due to rectal anal or cutaneous conditions to diabetes or to drug intolerance Proctitis with irritating discharge is an occasional cause Threadworms in the rectum pass into the anal canal for ovideposition and cause intense itching Piles and anal fissures are other common causes but cutaneous tags resulting from fibrosed piles should not be removed in an attempt to give relief On the skin lack of cleanliness monilial and fungous infections and *Phthirus pubis* infestation may be responsible or the condition may have arisen from sensitisation to local applications from drugs such as phenolphthalein taken internally from the disturbance of intestinal flora and the encouragement of monilia by the use of antibiotics such as chlortetracycline or chloramphenicol or rarely from skin diseases such as lichen planus Patients with pruritus ani often suffer from localised hyperidrosis which aggravates the condition by the discomfort it causes and by its encouragement of fungous and other infections In resistant cases without physical signs or with lichenification an emotional factor may be the most important this may take the form of inadequately expressed rage and aggression or it may be symptomatic of a passive homosexual tendency

Clinical Picture—The skin may look normal or there may be scratch marks and deep furrowing and ridging from lichenification There may be a sodden condition of the anal funnel or there may be a patch of lichen simplex 2 or 3 in to one side of the anus The psychogenic form may be accompanied by a tendency to exhibitionism shown by the wearing of effeminate clothing as well as by an exceptional enthusiasm for being repeatedly examined by the doctor

Treatment—If no obvious cause can be removed the treatment is symptomatic by bland local applications sedatives and in the most resistant cases X irradiation in exposures of 50 r or 75 r on up to four occasions at weekly intervals When lichenification is present thorium X applications may prove as effective as X rays and they carry no serious hazard of post irradiation skin changes The constant application of first one and then another remedy to the itchy anus must be discouraged as only increasing introspection A good standard of cleanliness is important but medicated soaps or antiseptics should not be used The skin should be dried carefully without friction from a towel and a dusting powder of talc and boric acid applied

The best local applications are hydrous ointment or a thin zinc cream to which 1 0 per cent of phenol may be added, or if any infective element is present magenta paint may give good results Antihistaminic creams and benzocaine derivatives are best avoided Good results are being claimed from the use of hydrocortisone ointment

Aperients, particularly phenolphthalein and aloes, may aggravate the condition and the patient should avoid them or use only liquid paraffin Strong coffee and condiments are best avoided

Psychoanalytical procedures are rarely of value in pruritus ani nor are nerve undercutting operations or anæsthetic injections a logical or effective procedure

SCROTAL AND PERINEAL PRURITUS

Here a fungous cause may be apparent There may be hyperidrosis Friction from clothing may aggravate the condition and sensitisation to dyed material may start it Pruritic scrotal dermatitis may also arise with diets deficient in protein iron and vitamin B complex but in the majority no local cause can be determined In psoriasis and lichen planus scrotal lesions may be present but they are rarely more than the local manifestations of the general disorder Lichen simplex is often observed with or without eczematisation and infective changes

Dietetic adjustments and antifungous measures may be indicated and disorders such as seborrhœic dermatitis lichen planus and psoriasis are treated on general principles For lichen simplex in the perineum or on the scrotum bland local applications such as oily calamine lotion or hydrous ointment are preferable to antihistaminic creams which have a tendency to sensitise the skin Local anæsthetic (benzocaine) applications have strong sensitising properties and may cause a severe eczematous dermatitis which adds to the patient s distress Thorium X in spirit in a concentration of 1500 e s u per ml, applied at fortnightly intervals on up to six occasions may help X rays may be used in fractional doses but are best avoided on the scrotum If they are used here it is wise to use very small (33 r) individual exposures up to a total of 100 r only

In addition to these local measures an attempt should be made to relieve sexual maladjustments if present This is more likely to succeed with scrotal than with perineal or anal pruritus

PRURITUS VULVÆ

This term is sometimes applied to dermatoses of the genitocrural region and medial aspects of the thighs, as well as more correctly, to strictly vulvar conditions

Ætiology and Pathology —The causes include vaginal discharges due to trichomonas or monilial infections, nutritional deficiencies drug intoxications particularly from oral chloramphenicol or chlortetracycline threadworms (in children) glycosuria psychosexual difficulties contact sensitisation to contraceptive jellies vaginal douche solutions or to the rubber of contraceptive appliances to lack of cleanliness or to the excessive use of antiseptics to *Phthirus pubis* infestation Localised dermatoses that may be responsible include psoriasis seborrhœic dermatitis lichen planus atrophic senile vulvo vaginitis Bowen s precancerous dermatosis but in all these conditions as well as in lichen simplex there is a possibility of the dermatosis being the result of friction rather than the cause of the pruritus A most intractable form is that due to *lichen sclerosis et atrophicus* this is an atrophic sometimes bullous condition of the vulva perineum and perianal skin often with similar lesions elsewhere

Clinical Picture —There may be no abnormal physical signs or there may be lichenification excoriation boils or impetiginous lesions or a superimposed mixed contact and infective dermatitis resulting from faulty treatment

Treatment —This depends on the cause and may consist of the control of diabetes or of a trichomonas infection the relief of an emotional conflict the removal

of an offending drug the avoidance of a contact irritant or the provision of an adequate diet A drug such as phenolphthalein may cause a fixed erythema at the vulva with pruritus or drugs such as chloramphenicol or chlortetracycline may by removing competitors encourage multiplication of monilia the pruritus in these circumstances being caused by a monilial vulvo vaginitis or by vitamin deficiency from the destruction of intestinal organisms having the property of synthesising vitamin B

Ample sedation with barbiturates is necessary to prevent the establishment of a vicious circle of friction lichenification and infection and more friction It must be remembered however that barbiturates can though rarely themselves cause pruritus vulvæ

Local treatment depends on the type of reaction observed If there is any infection magenta paint or Vioform cream are usually effective in the less severe forms due to monilia and *Staphylococcus saprophyticus* and a wide spectrum antibiotic such as chlortetracycline oxytetracycline or chloramphenicol in frankly pustular furuncular or impetiginous forms A 1 0 per cent solution of cetrimide is useful as a cleansing agent For vulvar boils the application of a 75 per cent industrial spirit with 1 per cent brilliant green and 0 1 per cent mercuric chloride is useful For lichen simplex hydrous ointment zinc cream or ether soluble tar paste (Martindale) may be used Antihistaminic creams are probably no more effective than the base in which they are incorporated and their use carries with it some risk of the development of cutaneous sensitisation Benzocaine anæsthetic applications are contraindicated because of their powerful sensitising properties The use of œstrogen creams is restricted to cases of senile vulvo vaginitis with atrophy For pruritus vulvæ with lichenification thorium X in a strength of 1500 e s u per ml of spirit applied fortnightly is sometimes effective as is X irradiation given in exposures of 75 r weekly on up to four occasions For Bowen s disease excision is preferable to radiotherapy owing to the relative radio insensitivity of this dermatosis

Psychogenic forms may respond to the relief of conflicts over sexuality these usually being due to a guilty liaison or to fear of pregnancy venereal disease or cancer

PRURIGO

Prurigo is a term used for a group of intensely itchy conditions in which the predominant physical signs are lichenification and excoriated papules Lichenification is produced by friction and presents as terracotta thickened skin with accentuation of the contrast between the normal diamond shaped elevations and intervening furrows Prurigo papules are ill defined obtuse elevations with excoriated tops caused by trauma from the finger nails In some forms a contributory factor may be erection of the hair follicles (horripilation) in response to various stimuli

Ætiology and Pathology—The ætiology of these various disorders will be dealt with individually

Histologically there is hyperkeratosis thickening of the granular layer and acanthosis with elongated rete ridges In the dermis there is an inflammatory infiltrate Areas in which the epidermis has been removed in part or in its full depth may be seen covered by blood scabs or by infected scabs

LICHEN SIMPLEX CHRONICUS

(PRURITUS WITH LICHENIFICATION NEURODERMATITIS CIRCUMSCRIPTA NEVRODERMITE)

Ætiology and Pathology—The sense of itching in this condition is usually central in origin and brought about by frustrated anger or libido or a trivial local irritant may operate in the first place and the vicious circle of itching rubbing lichenification itching be brought about This primary form has to be differentiated from lichenification developing on contact dermatitis a phenomenon not unusual where

compensation claims await settlement or where there is some other significant emotional factor in addition to a contact cause for a dermatosis In both primary and secondary forms hysterical traits are often apparent

Histologically there is slight hyperkeratosis and marked acanthosis, with a non specific infiltrate in the dermis

Clinical Picture —A patch of lichen simplex is usually oval and if on a limb lies in its long axis The colour is red or reddish brown and the edge fades off gradu ally into the normal skin without outlying " satellites The surface shows an accentuation of the normal skin pattern, creases being increased in both depth and width, and the interposing lozenge or diamond shaped areas more obviously elevated above the creases than in the normal skin These areas are often shiny and resemble grouped papules of lichen planus There may be a fine scaling or warty thickening If scratching is carried out as well as rubbing excoriations and blood scabs may be visible There is usually marked pigmentation but occasionally depigmentation occurs Lichenified skin is thickened and inelastic tending to become fissured and secondarily infected with erysipelas, impetigo or boils The sites most character istically affected by lichen simplex are the nucha the sides of the neck and the supra clavicular regions the ulnar aspects of the elbows, the hands the external genitalia the anal and perianal regions the inner and outer thighs, and the antero lateral aspects of the calves but other sites may be affected

Lichen simplex is modified in appearance in certain situations On the scalp scabbed excoriations are often seen or diffuse redness and profuse coarse scaling even with collarettes of coarse asbestos like scaling for a few millimetres up the hair shafts—the so called ' fausse teigne amiantacee At the nape of the neck an oval area is usually superficially excoriated with grey scales and light crusting A mild infection may be superimposed On the brows the hairs are broken off short On the palms dyskeratosis dominates the picture and accentuation of the skin pattern is inconspicuous In the flexures the hyperkeratotic skin becomes fissured sodden and whitened resembling leucoplakia The sufferer from lichen simplex may become agitated and start to rub the lesions during the interview when enquiry is made into relevant personal matters

Course and Prognosis —The malady may persist indefinitely or disappear with out treatment its relief depends on abatement of the emotional tension Sometimes this is not possible sometimes if the patient and the source of the tension can be separated the condition may clear without other treatment

Diagnosis —The diagnosis from lichenified dermatitis of external origin is often difficult Usually with lichenified dermatitis there is a history of a more widespread eruption which has finally become localised perhaps in the antecubital regions

Lichen planus may simulate lichen simplex but there are usually some discrete lesions to be found which clarify the diagnosis Lichenoid plaques on the legs how ever may be due to lichen simplex lichen planus or (rarely) lichen amyloidosis their differentiation may only be possible by biopsy

At the nucha, lichen simplex may resemble seborrhœic dermatitis and psoriasis, but the circumscribed pattern is not typical of the former and the absence of silvery scaling or of psoriasis elsewhere renders the latter diagnosis improbable The presence of pediculosis or of hair dye dermatitis must be excluded On the palms psoriasis and dyskeratotic contact dermatitis have to be excluded on the evidence of the history and the presence or absence of psoriasis elsewhere At the flexures leucoplakia can be excluded because it only occurs on mucous surfaces but lichen simplex of the mucosal aspects of the labia majora and of the labia minora may be accompanied by leucoplakia

Treatment —The treatment of lichen simplex is essentially the relief of the related tension state If as often happens this is not possible an attempt has to be made to break the vicious circle with general sedatives and local applications

Barbiturates are most useful for this purpose for example phenobarbitone gr ¼ to 1 twice a day and butobarbitone gr 3 to 4½ in the evening or a bromide and valerian mixture may prove useful and promethazine hydrochloride 25 mg in the evening for its antipruritic action Occasionally the draught of paraldehyde 1½ fl oz is indicated as a quick acting sedative for use in the middle of the night Amphetamine sulphate 5 mg after breakfast is useful when there is depression and helps the patient to obtain relief by deeds or words *in place of harmful and useless emotions*

Locally tar is of great value in the form of the solution of coal tar 2 to 6 per cent in zinc paste or the more elegant ether soluble tar paste (Martindale) may be used At the nucha it is better to incorporate the tar in the ointment of wool alcohols and when the skin is markedly thickened the solution of coal tar can be applied neat once a day with considerable relief At flexures and the anogenital region tar cannot be used with safety and magenta paint makes a valuable substitute partly no doubt from its phenol content and partly from its powers of controlling secondary fungous infections Occlusive dressings are not so effective as might be expected because *they may give the patient a feeling of guilt and frustration from the loss of the emotional* relief (*onanisme prurituque*) that rubbing these lesions provides

X rays in a course of three or four exposures of 75 to 100 r each time are often invaluable thorium X too 1500 e s u per ml is often helpful particularly at hairy sites or if the patch is of a shape and size not easily covered by an X ray applicator Thorium X is applied in spirit or as a varnish and the affected area should not be washed for the next 72 hours The patient should be warned that considerable pig mentation may develop at the treated site and persist for some months

The patient should avoid hot baths and proximity to fires and try to avoid emotional heat from the life situation as a whole Adjustments so as to avoid difficult personal contacts may be necessary and prove highly effective

PRURIGO OF BESNIER

(Flexural Prurigo Atopic Dermatitis Asthma Hay Fever Prurigo Syndrome Pruriginous Facial Eczema etc)

Prurigo of Besnier is an itching condition affecting in particular the flexures and the face it usually begins in infancy and may alternate with or more rarely be accompanied by asthma or hay fever

Ætiology and Pathology—The fundamental abnormality is spasm of plain muscle from many relatively trivial stimuli which would have little or no effect on the majority The spasm may affect the bronchioles causing asthma the vessels of the nose causing vasomotor rhinorrhœa and the skin causing gooseflesh and vasoconstriction Sweating is often excessive

Inheritance and the early environment both seem to be of importance in the ætiology but the latter seems more significant than the former Those affected are of average intelligence but are excitable and prone to feelings of insecurity and are often maladjusted to their parents particularly the mother (the so called maternal rejection factor) Threats to security or to loss of affection are the most significant and obvious of the many factors that bring about exacerbations Breakdowns may occur with changes of school or occupation or at times of engagement marriage or bereavements Other factors include changes of temperature or of humidity air borne injected or ingested allergens rough clothing drugs and infections The pruriginous individual reacts to everyday stimuli with a mechanism designed for emergencies Thus pollens danders and household dusts may cause bronchial spasm or vasomotor rhinorrhœa Stroking the affected skin causes a white line to develop in 15 seconds the usual red line does not follow at unaffected sites the normal reaction of white line followed by red may be observed Cutaneous infections in *these individuals tend to become generalised* in part because of the scratching that

helps dissemination Thus, pruriginous individuals may get generalised staphylo derma generalised herpes or widespread vaccinia

Clinical Picture —Besnier s prurigo presents as one of the forms of infantile eczema (*q v*) It may begin as early as the second month as a papulo vesicular and erythemato squamous condition involving parts easily reached by the infant—the face, neck, antecubital regions wrists hands, popliteal spaces calves ankles and feet The trunk may escape entirely or it may show a patchy ill defined faintly pink papular and scaly eruption The lesions may be exudative infected or lichenified

The infant periodically indulges in orgies of rubbing particularly in the evening when *bored, frustrated or tired, and with determination overcomes any attempt to* restrict this practice The face may be rubbed by rotation to and fro on the pillow even if the arms are tied The condition usually becomes milder when the child starts to walk and to do things for itself It may disappear for several years but there is usually a recurrence at puberty and the prurigo is then more strictly localised to the bends of the elbows and of the knees the hands and wrists the face and neck and sometimes to the genitocrural region and to the feet The affected areas show lichenification and excoriations The condition may persist well into adult life (though it usually gets less severe after 20 years of age) with exacerbations from exposure to heat anxieties and an ever varying pattern of contact sensitisers or air borne allergens (if the results of patch and scratch tests can be accepted as valid in these individuals) Sometimes the first occurrence is in adult life and engagement, marriage or a bereavement usually precedes the dermatosis

Xeroderma is often coexistent with Besnier s prurigo and modifies the picture Cataracts are a serious complication in some cases which persist into adult life They are believed to be congenital but friction applied to the eyelids may well play a part in their maturation

Course and Prognosis —This depends upon the possibilities of dealing with the causal factors If they cannot be eliminated the malady may persist indefinitely

Diagnosis —The malady has to be differentiated from contact eczematous dermatitis especially when complicated by lichenification In prurigo the essential lesion is not a papulo vesicle but is a prurigo papule an obtuse elevation of a brown or dusky hue often with an excoriated top or if these elementary lesions are not discernible lichenification dominates the picture

Besnier s prurigo involving the face (pruriginous facial eczema) has to be differentiated from actinic dermatitis and from eczematous dermatitis of the face caused *by air borne or hand transferred agents* The *former* affects the forehead nose and malar ridges and other parts exposed to light The latter affects particularly the eyelids and perhaps the skin of the sides of the neck

Treatment —The treatment of Besnier s prurigo is very much that of the whole patient with his characteristic personality and his personal problems rather than the management of his skin condition by itself A change of attitude and co operation on the part of the parents is equally important If a steadier level of affection in a calmer home atmosphere can be made to prevail all well and good If not a temporary removal from the unfavourable and often tense atmosphere is the second best choice *This may entail a period in hospital or in a convalescent* home and for some cases special residential schooling facilities are ideal

Apart from these procedures treatment is mostly symptomatic by bland local applications such as calamine liniment and general sedatives in ample dosage bearing in mind that sufferers from prurigo usually tolerate barbiturates well and need doses larger than the average to bring about quiet and sleep and freedom from scratching Antihistaminic drugs with antipruritic properties for example promethazine hydrochloride are also valuable Chlorpromazine 25 mg t d s or methylpentynol (Oblivon) 250 mg t d s is sometimes helpful The pruriginous patient needs to be kept fully

occupied either with suitable manipulative toys in childhood or by manual work in adult life

For the worst cases in patient treatment is invaluable sedation can then be used in larger doses and nonspecific measures tried such as fever therapy with T A B intravenously in doses of 25 million 50 million and 100 million organisms at 5 day intervals (for an adult) For localised patches thorium X or X irradiation is sometimes indicated Intravenous injections of corticotrophin 50 mg 8 hourly will bring about a partial remission but this treatment is advisable only in exceptional circumstances

Hydrocortisone ointment has recently been reported to be highly effective in relieving the local manifestations of this malady

DISSEMINATED NEURODERMATITIS

This term is used for extensive and severe examples of Besnier s prurigo and other widespread lichenified and pruriginous eruptions in which no contact toxic or reticulotic cause can be discovered but in which the malady appears to indicate a maladjustment to the environment particularly in circumstances of deprivation of occupational activities bereavement sexual frustration and unwantedness It affects adults of all ages

PRURIGO OF HEBRA (PRURIGO FEROX)

A chronic itchy disease starting as urticaria and persisting indefinitely Two forms are recognised prurigo ferox and prurigo mitis

Ætiology and Pathology —Inheritance is an important factor but whether this consists of the inheritance of an abnormality of the skin or a low level of intelligence is not clear probably the second is the more important

Clinical Picture —The condition usually begins in the first or second years with a polymorphic eruption of scratch marks erosions lichenification and papular urticaria The malady gradually becomes localised to the limbs particularly to their extensor surfaces Later prurigo nodules develop and the urticarial component fades

As years pass the picture is of extensive excoriations lichenification and pigmentation with scarring and thickening of the skin and freedom of the flexor aspects of the joints The lymph nodes in the axillæ and groins are enlarged The trunk neck and face may be affected The malady is rare in the British Isles

Diagnosis is from xeroderma and from other itchy diseases of the skin including crusted scabies

Course and Prognosis —Prurigo mitis may improve at puberty but in prurigo ferox the prognosis is unfavourable the malady persisting in spite of treatment Infection may occur

Treatment is symptomatic by bicarbonate of soda or tar baths antipruritic applications such as 2 to 4 per cent of solution of coal tar in zinc cream or paste and adequate sedation by bromides barbiturates or antihistaminic drugs A period of removal from the home surroundings to hospital convalescent home or residential school is often useful

PRURIGO NODULARIS

This is a rare malady and may in fact be a variant of lichen planus (*lichen obtusus corneus*) differing from *lichen planus hypertrophicus* by reason of the large obtuse dome shaped nodules affecting the extensor surfaces of the forearms and legs whereas *lichen planus hypertrophichus* is more plaquelike and usually localised to the calves and ankles

SECRETORY DISORDERS

Sweat secretion may be excessive, diminished or suppressed (hyperidrosis hypoidrosis and anidrosis)

Sebum secretion may be excessive (seborrhœa) or diminished (xeroderma ichthyosis) *Sebum secretion* is qualitatively altered in "seborrhœic dermatitis without there necessarily being any quantitative changes "Seborrhœic dermatitis may occur with an average sebum flow or with seborrhœa or even with xeroderma It is better designated "infective dermatitis

HYPERIDROSIS

Generalised sweating normally occurs from heat, exertion fear, febrile and toxic states Certain central nervous system lesions hyperthyroidism and acromegaly and some drugs (acetylcholine pilocarpine) can also cause sweating Adolescents and young adults are affected more often than children or older people by excessive sweating from anxiety the obese suffer most from heat and exertion

In localised hyperidrosis the sites most commonly affected are the palms and soles, the axillæ the anogenital region or the centre of the face On the palms and soles there is often also a tendency to perniosis Involvement of the hands may interfere with working capacity, owing to soiling of paper and other materials handled Sweaty feet provide damp dark poorly aerated conditions which are ideal for the growth of saprophytic organisms Sweat acid when secreted becomes alkaline as it decomposes and this further encourages the growth of pathogens and facultative pathogens, both bacterial and fungous The decomposing sweat often has an offensive odour (bromidrosis) and may become coloured from the proliferation of chromogenic bacteria (chromidrosis)

Excessive sweating predisposes to contact dermatitis from water soluble irritants Dermatitis in the rubber industry is more common in sweaty individuals the sweat leaching out potentially irritant antioxidants and other preservatives from the rubber Similarly, dermatitis of the axillary folds occurs from dyed clothing or from dress protectors

Perianal sweating often becomes complicated by maceration and monilial or other fungous infections

Axillary hyperidrosis is a serious inconvenience to many women because it may cause discolouration and rotting of fabrics bromidrosis and other social embarrassments Offensive axillary odour (bromidrosis) is entirely due to bacterial decomposition of the sweat the axillary apocrine sweat being without odour when first secreted

Sweating of the centre of the face may be caused in some individuals by eating hot or spicy foods

Excessive sweating in fever may cause the eruption of raindrop like vesicles (*miliaria crystallina sudamina*) situated in the horny layer

Treatment—The uncovering and removal of any emotional cause that may be present is essential for cure otherwise treatment is largely symptomatic A bromide mixture with belladonna to the limit of tolerance may be used to give temporary relief but is not a practical method for prolonged use Phenobarbitone may be more effective In severe cases a trial of ganglion blocking agents such as pentolinium tartrate is justifiable The fluid intake should be as small as possible consistent with the relief of thirst Frequent tepid baths should be taken and the whole body or the affected parts liberally dusted with a boric acid and talc or salicylic acid powder the latter being especially useful on the feet To prevent or combat infection and to minimise bromidrosis foot soaks in a 1 in 6000 solution of potassium permanganate

are useful Coarse woollen socks and rubber soled or tennis shoes should not be worn The socks should be of a cotton material and should be changed at least once a day For the axillæ a 1 in 80 solution of aluminium acetate (Burow s solution diluted 1 in 10 with water) is the most effective remedy The axillary hair should be kept closely shaven to make washing easier Sympathectomy is not advisable for a malady often emotionally produced and X ray treatment, if it is to be effective necessitates a dosage which exposes the patient to the risk of later irradiation effects on the skin

HYPOIDROSIS

Diminished sweating occurs in myxœdema congenital ectodermal defects extensive scarring diabetes renal disease and some cachectic states also in some skin diseases particularly xeroderma scleroderma and in the senile skin or in the atrophic skin following the administration of liquor arsenicalis or the excessive use of X rays or too much exposure to the sun In other skin diseases with pathological scaling partial obstruction of the sweat ducts may cause hypoidrosis

ANIDROSIS

Cessation of sweating occurs in the anæsthetic skin areas of leprosy after sympathectomy and sometimes in poliomyelitis Sweat suppression may occur in hot humid climates as prickly heat (*miliaria rubra*) and as tropical anidrosis (*miliaria profunda*) In temperate climates a similar condition may be caused by hot humid working conditions and by exposure to moderate heat after having suffered and perhaps partially recovered from some forms of contact dermatitis for example that due to cement dust

Prickly heat is peculiar to the white races Its causes are believed to be the wearing of clothes and the use of spirit powders and too much soap on the skin in humid hot climates also the seborrhœic type of skin with follicular vulnerability to infection The qualitative sebaceous deficiency leads to the formation of keratin rings at the ostia of the sweat ducts These rings act as plugs and the dammed up sweat bursts out from the ducts causing disruption of the adjoining epidermal cells rupture of the duct lower down may cause an inflammatory reaction in the dermis Clinically there are itchy red papules of prickly heat (*miliaria rubra*) and follicular pustules (*ostio folliculitis* Bockhart s impetigo) due to infection of the contents of obstructed ducts Recurrent attacks of prickly heat may lead to destruction of the intra epidermal portions of the sweat ducts further exposure to heat and humidity may then lead to *miliaria profunda* with vesicles resembling sago grains in the dermis causing non itchy tropical anidrosis which may go on to heat stroke

Adhesive plaster skin reactions are more often due to sweat duct obstruction and infection than to eczematous hypersensitivity It usually starts 48 hours or more after the application of the plaster It is likely that other forms of dermatitis for example those due to dress protectors rubber cement etc are in part due to sweat duct irritation and obstruction

Prevention and Treatment—An attempt should be made to maintain an oily film on the surface of the skin in order to replace any sebaceous deficiency For this purpose anhydrous lanolin or the ointment of wool alcohols may be used The patient should be advised against the use of degreasing and dehydrating substances on the surface of the skin and should wear loose mesh cotton underwear

DYSIDROSIS (see Pompholyx p 1220)

SEBORRHŒA

Excessive oiliness of the skin may occur from puberty onwards and is due to *hormonal (androgenic) influences*, it usually diminishes with advancing age It is more common in the coloured races and may show a familial incidence amongst white people It affects the regions with most sebaceous glands, the scalp the face the nasolabial folds the chest and the back The skin is greasy, thickened, muddy coloured and with patulous follicles from which semi solid sebaceous material is extruded There is often a tendency to premature baldness of masculine type while other areas, such as the beard and chest grow tough, coarse hair *Acne vulgaris* is a common complication of seborrhœa Keratinous plugs at the pilosebaceous follicles cause retention of sebum and inflammatory changes of acne papules and pustules Infection of the seborrhœic skin with facultative pathogens may cause infective (seborrhœic ') dermatitis or *infection with more virulent organisms may* cause impetiginised seborrhœa or furunculosis The seborrhœic skin is unduly susceptible to fat soluble irritants, hence the application of ointments containing antiseptics may cause a chemical folliculitis and dermatitis Seborrhœic individuals have a tendency to develop rosacea

Treatment—The diet should contain ample protein vitamins and minerals and should not contain an excess of fats and carbohydrates Frequent washing with *soap and water is essential Sulphur compound lotion may help to diminish seborrhœa* and to control any associated acne or infection

XERODERMA

In xeroderma and its more severe form ichthyosis the skin is abnormally dry *with a diminished secretion of sebum and to a lesser extent of sweat* There is also a thickening of the horny layer sometimes with preference for the pilosebaceous follicular orifices (*Keratosis suprafollicularis*)

Ætiology and Pathology—The disease is inherited apparently as a dominant factor affecting both sexes and often several members of one family It is usually noticed soon after birth and may be present at birth Histologically there is hyper keratosis especially at the pilosebaceous ostia and an absence of the granular layer The prickle *cell layer is thin The sebaceous glands are few and small* but the sweat glands are not obviously diminished

Clinical Picture—In the milder cases the skin on the extensor surfaces of the limbs and body is dry and rough, with a slight branny scaling The flexures appear normal On the extensor surfaces of the limbs the hair follicles are prominent with small horny spines projecting The hair is dry and lustreless and breaks easily It may be sparse In severer cases fish like adherent grey scales cover the whole body *The skin is rough and even the face is affected to some extent* *Ichthyosis hystrix* is a form of hard nævus occurring in lines or bands and has no relation to ichthyosis Xeroderma often accompanies Besnier s prurigo

Course and Prognosis—The dry unoiled skin cracks easily and from its deficiency of sebum is susceptible to bacterial infection Xerodermatous *individuals* have to be prevented from taking up unsuitable occupations Excessive contact with soaps detergents and fat solvents are all likely to be harmful exposure to cold weather aggravates the condition the glandular activity then being minimal on the other hand extreme heat may lead to heat stroke owing to the inability of those suffering from severe xeroderma to lose heat adequately by sweating Xerodermatous individuals should be in clean dry work in an equable temperature Xeroderma tends to improve to some extent at puberty only to get *worse again* with advancing age The worst cases remain severe in adult life

Diagnosis—This is usually easy Differentiation has sometimes to be made from acquired atrophy with scaling of the legs or from phrynoderma (*keratosis follicularis*) caused by vitamin A and C deficiency The history and the distribution of the dry but not inflamed skin usually enables the correct diagnosis to be made

Treatment—Warm baths may be taken daily followed by the rubbing in of a suitable ointment Individual preferences vary Some like to rub in soft paraffin ointment while the skin is still moist others prefer the ointment of wool alcohols or glycerin of starch with either hydrous lanolin or salicylic acid ointment in equal proportions A superfatted soap should be used but not to excess The administration of thyroid extract or of vitamin A is without effect

PIGMENTARY ANOMALIES

The colour of the skin depends on the amount of skin pigment (melanin) it contains on the thickness of the epidermis and on the amount and oxygen content of the blood flowing through the more superficial vessels of the dermis The muddy colour of acne is related to the relatively opaque thickened horny layer and increased sebum flow the patchy redness of rosacea to the static dilatation of the cutaneous vessels and the peachlike skin of the maiden to her naturally thin and smooth relatively translucent feminine horny layer overlying blood vessels neither statically dilated nor contracted but responding normally to changes of temperature and of mood The colour of the skin is a poor index of the hæmoglobin content of the blood If the blood vessels of the skin are dilated anæmia may be masked and if they are contracted there may be considerable pallor without anæmia

Pigmentary changes in the skin may be due to an excess or insufficiency of melanin or to the presence of extraneous substances including blood pigments bile pigments carotene mepacrine gold silver lead bismuth and various substances introduced in tattooing either by accident or intention

PHYSIOLOGY OF MELANIN FORMATION

Melanin a complex iron free substance is formed in the melanoblasts by the action of a ferment dopa oxidase on a colourless precursor dihydroxyphenyl alanine (dopa) dopa is formed from tyrosine by tyrosinase but only in the presence of copper Melanin synthesising cells (melanoblasts) can be differentiated from melanin containing cells (melanophores) by the dopa reaction fresh tissue is immersed in a solution of lævo rotatory 3 4 dopa when the melanoblasts are stained brown Reducing substances for example ascorbic acid inhibit melanin formation and oxidising agents stimulate it Dimercaprol (B A L) and thiouracil may inhibit pigment formation a may the monobenzyl ether of hydroquinone when applied locally

Melanoblasts are dendritic cells scattered amongst the germinal epidermal cells of the basal layer The melanin is carried by their dendritic processes to the cells of the basal and prickle layers and deposited as granules within them Pigment containing cells (melanophores) are also seen in the dermis they take up any melanin that passes from the epidermis to the dermis Increased melanotic pigmentation of the skin may occur with or without previous inflammation of the skin and may be general or local

INCREASED PIGMENTATION

Racial pigmentation affects the buccal mucosæ as well as the skin Without prior knowledge of the inheritance it is sometimes difficult to decide if pigmentation is racial but a consideration of the colour of the eyes and the colour and texture of the

hair together with other racial anatomical traits of facies etc usually prevents error

Physiological pigmentation—In pregnancy there is patchy facial pigmentation (*chloasma uterinum*) linea nigra in the midline of the abdomen and darkening of the nipples and genitalia, often as an early diagnostic feature

Congenital forms include pigmented, fleshy hairy moles, lentigines and ephelides or freckles The mongolian spot is a blue black discolouration of the skin often in the sacral region, and is a deeply situated mole In neurofibromatosis (von Recklinghausen's disease) there are pigmented patches on the skin which may precede the development of tumours by many years

Ephelides (*Freckles*)—These are pale brownish macules which become darker after exposure to sunlight They are seen particularly in sandy or red headed persons and those with ancestors of these colourings

Histologically the only change is an increase of pigmentation in the basal layer

Treatment is preventive by the wearing of broad brimmed hats and the use of sun screening creams Attempts at removal of freckles by peeling agents are hazardous and may result in dermatitis

Lentigines (*Non hairy Moles*)—A lentigo is a dark brown macule which does not change colour after exposure to sunlight

Histologically there is excessive pigmentation of the basal layer and an increase of clear cells The rete ridges are elongated and club shaped The basal cells may appear somewhat disorganised but the *epidermo dermal junction* is well defined Nævus cells are not present in the dermis

Course and Prognosis—Lentigines are seen in children but they become much more numerous after puberty and in pregnancy It is not uncommon for hundreds to be present on one person Lentigines are potential melanomata but malignant change occurs only in a very small proportion of them The stimulating factors appear to be the endocrine changes of puberty and pregnancy and physical traumata At certain sites malignant proliferation is much more common than at others These danger sites include the paronychial and subungual regions the soles the lower limbs more than the upper limbs and their distal parts more than their proximal parts clothing friction sites on the body and the face For this reason it is sometimes advisable prophylactically to excise lentigines on the soles or at friction sites before puberty or early in pregnancy For the rest treatment is not necessary but if for cosmetic reasons it is desired to remove a lentigo from the face it should be properly excised in full depth and not subjected to destructive cauterising or freezing procedures which may lead to activation of any cells that remain

Fleshy hairy moles—These are dealt with elsewhere (see Tumours)

Increased pigmentation from physical causes—The skin responds to light X irradiation heat and friction by increased pigment formation This may be seen as sun tanning and the effects of ultra violet baths pigmented macules are often present in the periphery of scars of lupus treated with the Finsen Lomholt lamp and prolonged solar irradiation leads to the condition of poikiloderma in which there are telangiectasia atrophy and macular pigmentation and depigmentation an identical condition to that occurring after excessive X irradiation A similar appearance also occurs in the rare congenital malady xeroderma pigmentosum in which there is an inborn susceptibility of the skin to light

Long continued exposure to tar or creosote causes pigmentation of the parts exposed to light the tar apparently being a light sensitiser Bergamot oil, too in creams or perfumery may cause pigmentation There may be mottled pigmentation of the face with some telangiectasia when creams are responsible or a necklace like line of pigmentation from beneath the ears around the neck when *Eau de Cologne* placed behind the ears has trickled down or been carried down in the sweat (berloque dermatitis) A similar pigmentation may occur after thorium X is applied to the skin

Certain plant juices have a photosensitising action (phytophoto dermatitis) par

ticularly wild parsnips figs the common rue and limes also convolvulus and agrimony and even the buttercup and bindweed A severe inflammatory reaction precedes the pigmentation

Heat may cause the condition known as erythema ab igne a network of pigmentation involving areas of skin corresponding to vascular anastomoses

Friction may cause pigmentation at truss hatband and other sites of clothing contact also in rubbed areas of itchy skin for example in pediculosis (vagabonds disease) prurigo lichen simplex etc

Certain dermatoses particularly lichen planus lichen simplex dermatitis herpetiformis and exfoliative dermatitis (erythroderma) are often accompanied or followed by much pigmentation In urticaria pigmentosa the pigmented macules urticate on friction Incontentia pigmenti is a peculiar reticular and mottled pigmentation of infants and is thought to be the end stage of an inflammatory process of unknown cause In pityriasis (tinea) versicolor the brown lesions are slightly scaly

Toxic pigmentation occurs from certain drugs for example arsenic which causes a raindrop effect of white spots in a dark background with skin coloured pinhead palmar and plantar keratoses and dirty grey keratoses more widespread on the trunk often leading to skin cancers Organic arsenic does not have this effect but may cause exfoliative dermatitis and secondary melanosis

Endocrine metabolic and nutritional disorders—In Addison s disease there is a diffuse pigmentation of the skin with involvement of the buccal mucosæ Pigmentation also develops *very often during treatment with corticotrophin* Diffuse pigmentation may occur in liver disease abdominal tuberculosis malignancy malaria diabetes and thyroid disorders In Gaucher s disease (kerasin lipoidosis) there is brownish discolouration of the skin In pellagra the skin is deeply pigmented on the parts exposed to sunlight particularly the backs of the hands probably from the absence of reducing substances which normally check excessive pigmentation on exposure to light There is also diarrhœa and dementia and often other evidence of malnutrition

Acanthosis nigricans (*q v*) presents as velvety skin piling up in folds particularly in the flexures

DIMINISHED PIGMENTATION

Racial differences in degree of pigmentation depend on varying physiological activities of the melanoblasts which are present in all races in approximately the same concentration

Albinism—In this condition there is a genetic lack of the enzyme tyrosinase a copper protein complex in which the copper plays an essential catalytic role

Vitiligo—*Vitiligo is the commonest form of depigmentation* There is a macular discoid and figurate depigmentation of the hands face genitalia or other regions On the scalp the hair may be white in the affected areas (leucotrichia)

Ætiology and Pathology—The ætiology is obscure Histologically melanoblasts are as numerous in the pale areas as in the darker surrounds but the melanoblasts in the pale areas are inactive (dopa negative) and they and the melanophores are deficient in pigment whereas those in the adjoining darker areas contain an excess

Diagnosis has to be made of this primary leucoderma from secondary leucodermas due to eczema psoriasis lupus erythematosus syphilis leprosy scleroderma or pityriasis versicolor

In eczematous or psoriatic leucoderma there is a history of a past inflammatory stage in vitiligo only of pale areas which redden but do not tan in sunlight In syphilitic leucoderma colli there are other manifestations of syphilis the lesions are uniformly small and confined to the neck and there may be some cutaneous atrophy which is absent in vitiligo

In leprosy the colour contrasts may not be so marked as in vitiligo, the pale areas are anæsthetic to light touch and differences of temperature, and thickened nerves can be felt serving the area or some other situation for example the neck the ulnar side of the elbow or the popliteal space When these nerves are rolled under the fingers the patient may experience paræsthesia but no pain in the area they supply The pale areas may be anidrotic

In scleroderma or its localised form morphœa there is increase of substance and marked hardening in the pale areas but no loss of sensation In scars and scarring diseases of the skin there is often depigmentation whether the scars are hypertrophic, normal or atrophic

In tinea versicolor the brown areas are "islands", the white areas the 'sea around In vitiligo the opposite applies the white areas being 'islands' in a 'sea of browner skin But the diagnostician has to be wary of certain exceptions to this rule Vitiligo may become so extensive that there is more pale skin than dark and in these circumstances brown areas may seem to represent 'islands' but if they do, their coastlines will be a series of bays or concavities indicative of the condition spreading from pale to darker zones In the form of vitiligo known as leucoderma centrifugum acquisitum (Sutton s disease) there is an intensely pigmented macule surrounded by a pale area beyond which is skin rather more brown than normal and beyond this normal skin

When skin affected with tinea versicolor is exposed to the sun the affected areas do not pigment as well as the normal skin around so that a photographic negative of the original malady is produced (*achromia parasitica*) In coloured people too, the affected skin of tinea versicolor is paler than the normal skin nearby The diagnosis is established in all doubtful cases by the more characteristic distribution of tinea versicolor on the trunk and by the discovery of spores and mycelial threads on scraping the lesions and direct microscopic examination of the material in potassium hydroxide

Leucoderma can arise from contact with rubber the responsible chemical being the monobenzylether of hydroquinone used as an antioxidant Clinically this type may be indistinguishable from the idiopathic form

Treatment—Meladine is said to bring about repigmentation It is the refined products of the plant *ammi majus linn* It is taken internally and applied on the surface the skin also being exposed to ultra violet rays Repigmentation begins around the hair follicles and it is probably only successful in those cases of vitiligo with pigmented hairs growing from the white skin such cases have melanoblasts in their hair papillæ which are still capable of responding to stimuli

NONMELANOTIC PIGMENTATIONS

Hæmochromatosis is a bronzed pigmentation which may involve the mouth there is diabetes and enlargement of the liver

Hæmosiderosis results from blood pigments which may be deposited in eczema and dermatitis involving the lower limbs in the capillaroses (Schamberg s progressive pigmentary dermatosis Majocci s purpura annularis telangiectodes lichenified and disciform pigmentary dermatosis of Gougerot and Blum angioma serpiginosum of Hutchinson)

The lemon yellow to brown pigmentation of jaundice is due to bile pigments in various concentrations Jaundice can be differentiated from racial pigmentation and other forms due to melanin by the involvement of the conjunctivæ the conjunctivæ are not tinted in mepacrine pigmentation when this drug is taken in therapeutic doses

Mepacrine pigmentation slowly develops with the daily ingestion of 0 1 to 0 3 g of the drug and the discolouration may take a month or two to fade after the drug is withdrawn The pigmentation of lichenoid mepacrine dermatitis is melanin

Carotinæmia due to the excessive ingestion of carrots produces an orange tint mo t marked on the palms The conjunctivæ remain white

Metallic intoxications—Lead causes a blue black line on the gums opposite areas of marginal gingivitis or caries owing to the deposition of lead sulphide Silver may if ingested or applied to the eyes or mucous surfaces be absorbed and cause localised or general argyria which gives a slaty blue colour to the skin due to local deposition of the metal A secondary melanoderma due to the irritating effects of the silver on the melanobla ts also may occur Gold may become deposited in the skin (auriasis) giving it a brownish colour or may if it causes a lichenoid or exfolia tive dermatitis result in much increase of melanin formation Bismuth may cause a black line on the gums but does not affect the skin except secondarily either gener ally by the rare occurrence of exfoliative dermatitis or locally when the injection is accidentally given too superficially and a white foreign body reaction occurs with ulceration through the skin which may persist for months and end in ugly scarring

TATTOOING

Tattooing may be accidental or intentional In the accidental form explosive materials coal dust or road surface materials are usually responsible In the inten tional form when tattooing has been used for identification purposes only one colour has been used but various pigments may be used when the purpose is display The blue black colour owes its bluish tint to the effects of the overlying dermis the pigment being some form of carbon iron oxide or logwood The colour red is due to cinnabar (mercuric sulphide) and is important because it may be the cause of allergic reactions and may also modify the development of a syphilitic dermatosis owing to the spirochæticidal effect of the mercury A green colour may be produced by chrome oxide hydrated sesquioxide or phthalocyanide dyes a yellow by ochre or by cadmium yellow but this has a bad reputation for causing blistering on sub sequent exposure to light

Tattooing has been responsible for inoculating syphilis tuberculosis vaccinia and virus hepatitis psoriasis and lichen planus may be set off in tattooed areas

Tattoos may be removed by excision with or without grafting or by various methods destructive to the dermis including carbon dioxide snow caustics and abrasives

PIGMENTED TUMOURS OF THE SKIN

These include moles melanomata Mongolian spots basal cell carcinomata keratoses juvenile and senile (seborrhœic) warts leiomyomata fibromata Darier s disease and acanthosis nigricans (*q v*)

VASOMOTOR DISORDERS

ERYTHEMA PERNIO (CHILBLAINS PERNIONES ERYTHROCYANOSIS ACROCYANOSIS)

A condition of bluish red cold skin of exposed parts with swelling and itching caused or aggravated by exposure to damp cold

Ætiology and Pathology—The chief cause is damp cold operating on a skin which is by inheritance oversensitive to its influence Arteriolar vascular spasm results with anoxæmia of the affected parts at first intermittent later chronic The blood stagnates in the statically dilated venules leading to œdema degeneration and fibrotic thickening of the connective tissue and of the vascular endothelium itself

Puberty is the time of worst involvement Insufficient exercise is an important factor (or paralysed muscles as in poliomyelitis) The outward application of heat *to the chilled surface aggravates the condition* Thromboses or extravasation of blood may occur, leading to ulceration

Clinical Picture —Perniosis may affect any area exposed to cold particularly the distal parts of the limbs the nose and the ears Involvement of the upper limbs is usually confined to the digits but on the lower limbs the calves are affected as often as the feet

Chilblains are far commoner in females than in males a fact only partly explained by their more scanty clothing The more sedentary tasks often carried out by women in cold draughty *or even damp surroundings are also partly responsible and it is* probable that some unexplained endocrine factor is of importance Chilblains present as bright pink or bluish swollen, non pitting areas of skin Blotchy redness is present at one area blueness at another The blue areas become red temporarily after gentle massage from the periphery Chilblains often itch severely and may feel warm to the finger in this red swollen stage but later when the vessels have become statically dilated as on the legs of young women (*erythrocyanosis crurum puellarum frigida*) the affected parts feel cold and are deep blue in colour except where casual contacts have emptied the superficial vessels Often the blue discoloration is most marked around the hair follicles If the œdematous process is marked bullæ may develop and on rupturing leave ulcerated chilblains Fissures (chaps) form on the fingers and hands and infection may lead to cellulitis

Course and Prognosis —Individual attacks resolve with the coming of more clement weather or with better precautions against damp cold, but each attack leaves the tissues less able to withstand cold in subsequent winters

Diagnosis —On the face and hands chilblains have to be differentiated from lupus erythematosus profundus (lupus pernio of Hutchinson) This may be extremely difficult except after a period of observation Lupus erythematosus persists in warm weather childblains do not

On the face and hands chilblains also have to be differentiated from sarcoidosis *(lupus pernio of Besnier) a persisting doughy bluish swelling of* the nose, ears or digits The histology will help if doubt exists on clinical grounds

On the legs perniosis has to be differentiated from Bazin s disease and from Darier Roussy subcutaneous sarcoids Both of these conditions occur in individuals with perniotic circulations but in addition there are extensive areas of hard bluish nodulation perhaps with deep and extensive ulceration

Erythema multiforme may cause lesions resembling chilblains on the fingers but the palms are also often affected and characteristic target *lesions may be seen*

Treatment —Once it is known that there is a tendency to chilblains every effort should be made to prevent aggravation by suitable warm clothing all over the body as well as to the affected part by proscribing the sudden application of heat to the affected part by attention to bad housing by draught elimination duck boarding on stone floors etc by adequate exercise and the avoidance of standing or sedentary jobs by warming the affected parts by exercise of the whole body or by the gradual and diffuse application of warmth with massage to help the venous *blood flow* An electric blanket is preferable to a hot water bottle

Drugs hold a minor place in the treatment of chilblains and it is important to make the patient realise that alleviation depends much more on the *correction* of faulty habits than on medicines Thyroid may be prescribed if there is any evidence of hypothyroidism A temporary increase in the blood flow to the extremities may be brought about by tablets of nicotinamide 50 mg or of tolazoline hydrochloride (Priscol) 25 mg Calcium has for long had a reputation for relieving *chilblains* by some means as yet unexplained it is best prescribed in tablet form with vitamin D_2 The use of massive doses of vitamin D_2 for the control of chilblains is

inadvisable in view of the possible serious side effects General ultra violet and infra red irradiation may help

For unbroken chilblains calamine liniment may be rubbed in from the periphery For fissures the ointment of wool alcohols is comforting Appropriate antibiotics may be required to control secondary infections

ROSACEA (ACNE ROSACEA)

This condition is primarily erythematous and secondarily papular it is characterised by lability of the facial blood vessels going on to persistent static dilatation and to congestive hypertrophy and inflammation of the pilosebaceous follicles sometimes ending in necrosis

Ætiology and Pathology—Rosacea is essentially a state of vasolability of the face particularly the centre of the forehead the nose the fronts of the cheeks and the chin The vessels respond excessively to emotional stimuli to changes of temperature and to gastric irritants The gastric vessels and musculature tend to be hypotonic but there is no uniform change in gastric secretion as shown by test meals Hormonal (menopausal) influences are sometimes important

The rosaceous patient is characteristically obsessional with very high standards of conduct and much resultant anxiety if these standards are not maintained Excessive (often self imposed) activities and insufficient time for meals result in a sense of hurry flatulent dyspepsia and flushing of the face Anger if habitually repressed may also cause flushing of the face as may feelings of shame or embarrassment A seasonal exacerbation in the early spring is sometimes noted

Histologically there is vascular dilatation and focal inflammatory nodules either of lymphocytes or of tuberculoid type with lymphocytes epithelioid cells and giant cells There may be some perifolliculitis and abscess formation and all degrees of hyperplasia of the sebaceous glands from a moderate degree in papular rosacea to an extreme degree in rhinophyma In the latter condition there is also fibrous hyperplasia

Clinical Picture—The patient is usually a woman aged between 30 and 50 but men also are often affected and adolescents of either sex may suffer from this malady The patient complains of redness and pimpling of the face with aggravation from exposure to extremes of temperature from hurry anger embarrassment or general anxiety from hot drinks or indigestible foods or in the premenstrual tension phase There may be a flatulent dyspepsia At first there is only a tendency to flush or blush easily later the redness becomes persistent telangiectases being visible and finally red pimples form which may suppurate or necrose giving rise to crusted papules which end in depressed scars There are no comedones but sometimes acne vulgaris coexists more commonly acne at puberty is succeeded by rosacea some years later Patients with rosacea usually show evidence of the seborrhœic state with all its consequences Conjunctivitis blepharitis keratitis and corneal ulceration may all complicate rosacea

Rhinophyma is a rare disorder and much more common in men than in women Irregular fleshy masses develop on the distal two thirds of the nose with visibly enlarged follicular orifices

Course and Prognosis—Rosacea is amenable to treatment provided the patient is willing and able to co operate with the physician A variable amount of scarring may be left The eye lesions may cause serious impairment of vision

Diagnosis is from acne vulgaris lupus erythematosus contact eczematous dermatitis and polycythæmia In acne vulgaris the distribution is different the face is muddy not red and comedones are present In the rosaceous form of lupus erythematosus atrophy can be discerned and the eruption is worsened by exposure to the

sun Contact eczematous dermatitis may coexist It presents with ill defined areas of redness and peeling at various sites on the face, particularly the eyelids around the mouth and on the neck In polycythæmia the whole face is persistently plum coloured

Treatment—All circumstances that are likely to bring about flushing of the face have to be avoided Exposure to cold winds, fires or for that matter the kitchen stove have to be avoided as far as possible Hot drinks too are harmful particularly excessive hot tea drinking and they are a more common cause of exacerbation than alcohol, condiments or indigestible food Obsessional traits have to be moderated if possible Adequate time must be allowed for meals which should have ample protein and vitamin content with no excess of fats or carbohydrates The patient must be encouraged to express hostility more naturally More fundamental psycho logical factors are on the whole, best left undisturbed because the patient with rosacea usually cannot tolerate this line of approach

Rosacea is not related to nutritional deficiency except secondarily through the associated gastric disturbance Vitamin B complex and iron are sometimes indicated, and it is always wise to estimate the hæmoglobin content of the blood Internal treatment also consists of sedation gastric ' tonics ' and when necessary œstrogens A useful medicine before meals is sodium phenobarbitone gr ½ in either the acid or the alkaline gentian mixture Sometimes an acid mixture seems to be more helpful sometimes an alkaline one Fractional test meals show marked variations from one rosaceous patient to another and for that matter, in the same patient on different occasions hence they are of little value in deciding on the best medication Bromides and iodides should not be given to rosaceous individuals as they may grossly aggravate the condition

Œstrogens are sometimes indicated for example ethinyl œstradiol 0 05 mg twice a day for 10 days preceding each monthly flow, or the same remedy may be given once daily for up to 3 months to post menopausal women

Local treatment is relatively a secondary matter Zinc sulphate lotion or calamine lotion with 1 per cent of sulphur or of ichthammol, may be used The patient must not wash the face in very hot or very cold water and should not manipulate the lesions Occasionally the lesions become infected, and then need treatment with the appropriate antibiotic

In patients with sebaceous hypertrophic nodules X ray exposures 150 r weekly on up to four occasions may help

In rhinophyma the large masses may be reduced by X ray exposures of 250 r each up to a total of 1000 r but surgery is better the lesions being pared down with a scalpel or razor under general anæsthesia until the normal contour of the nose has been regained bleeding being controlled with the galvano cautery

For the conjunctivitis the zinc and boric eye lotion is useful Keratitis needs the attention of an ophthalmologist Bright light must be avoided Homatropine drops are indicated and cortisone drops give great relief

RAYNAUD S PHENOMENON

This is described on p 922 It may occur with perniosis lupus erythematosus or scleroderma

ERYTHROMELALGIA

This is a persistent painful warm redness of the extremities It is dealt with elsewhere (see p 924)

DERMATITIS DUE TO PHYSICAL CAUSES

Dermatitis may be caused by heat or cold maceration or drying ultra violet irradiation X rays thorium X or radium and by mechanical causes including friction and pressure

DERMATITIS DUE TO HEAT

ACUTE HEAT EFFECTS —These are those caused by dry heat (burns) and moist heat (scalds) and are dealt with at length in surgical textbooks Suffice it here to say that a first degree burn (erythema only) arises when the heat causes drying of the surface but insufficient damage to lead to exudation into the skin The treat ment consists of the application of a bland animal fat such as lanolin preferably mixed with mineral oils as in the ointment of wool alcohols

In a second degree burn there is erythema and blistering with a risk of infection once the blisters are broken and of loss of protein and electrolytes if the blistered area is extensive Intact blisters should be punctured under aseptic conditions allowed to collapse and then covered with a gauze dressing The roofs of ruptured blisters should be cut away and the raw area swabbed with a 1 per cent solution of cetrimide in a sweeping centrifugal action Tulle gras dressings enable healing to proceed with the minimum of trauma to the young granulation tissue

The treatment of third degree burns is a surgical matter

ELECTRIC BURNS —Electric burns are often painless aseptic and dry but slow in healing The treatment is similar to that of other burns

CHRONIC OR RECURRENT HEAT EFFECTS —This causes the condition known as erythema ab igne often seen on the legs of women There is a pigmentary network corresponding with the sites of anastomoses between adjoining venous areas

CLIMATIC HEAT EFFECTS —Miliaria rubra (prickly heat) (See Anidrosis)

DERMATITIS DUE TO COLD

PRURIGO HIEMALIS —An itching eruption occurring only in the winter usually confined to the legs sometimes affecting the forearms and thighs Changes of temperature for example undressing hot baths sitting near fires precipitate the itchy episodes The lesions are inconspicuous patchy mild lichenification and scratch marks and marked dryness of the skin

Treatment consists of the avoidance of extremes of temperature and of the excessive use of soap Calamine liniment is helpful

LIVEDO RETICULARIS —This is a condition in which the legs show a livid network of venules the network corresponding to the anastomoses between the adjoining venous areas

CHILBLAINS —A chilblain is a static dilatation of venules secondary to anoxia caused by arteriolar spasm (see Vasomotor Disorders)

IMMERSION FOOT (TRENCH FOOT) —This is due to prolonged exposure to cold water insufficient to cause frostbite The feet are white red or cyanotic The patient complains of numbness and cramp Minor injuries may cause gangrene On removal from the cold a red swollen blistery hyperæmic stage develops unless the parts are very slowly warmed

Treatment is by gradual warming cleansing and elevation of the limb followed by exercise and the application of salicylic acid dusting powder

FROSTBITE (DERMATITIS CONGELATIONIS) —This is due to freezing of the soft tissues with cessation of the blood flow On thawing there is an erythematous a bullous or a gangrenous reaction

Treatment is by very gradual defrosting and treatment of the damaged tissue on recognised surgical lines

DERMATITIS DUE TO ACTINIC RAYS

ACUTE SOLAR DERMATITIS —This arises from excessive exposure to the sun and may occur in all degrees of intensity as with heat burns It is treated on similar lines

CHRONIC SOLAR DERMATITIS —Repeated exposures to the sun cause premature changes of ageing in the skin The physical signs consist of atrophy with telangiectasia pigmentation and depigmentation and a tendency to form keratoses It is *sometimes called 'farmers' skin' or 'sailors skin'* and is seen on the face and on the backs of the hands, rarely also on bald heads Another condition sometimes known as 'peasants skin , occurs on the back of the neck in the form of lozenge shaped pink thickened areas of skin (see Dermatitis rhomboidalis nuchæ)

ECZEMA AB SOLARE —This condition of hypersensitivity to light may present in many forms hence the term 'polymorphic light eruption The same individual in one attack may show eczematous features and in another pruriginous ones The lesions are on the forehead, cheeks ears and exposed parts of the neck and limbs Many substances applied to the skin have a light sensitising effect These include tar bergamot oil, acriflavine sulphonamides and eosin Dermatitis bullosa striata pratensis is a bullous dermatitis of exposed parts coming on after contact with a light sensitising plant followed by exposure to the sun (phytophoto dermatitis) Various plant juices including lime, figs rue wild parsnips, etc, may have this effect Some drugs also have light sensitising effects particularly sulphonamides and other drugs having hepatotoxic properties

PRURIGO ÆSTIVALE —This occurs in children and is a papulo erythematous rash on the exposed parts which recurs only in summer months

HYDROA ÆSTIVALE VEL VACCINIFORME (HUTCHINSON S SUMMER PRURIGO) —This severe bullous eruption of the exposed parts recurs each summer most commonly in boys and is associated with congenital hæmatoporphyria It results in pock like scarring

XERODERMA PIGMENTOSUM —In this rare malady there is an inborn over sensitivity to ultra violet and visible rays and, as a result senile atrophic changes resembling radiodermatitis develop at an early age and the sufferer may in adolescence begin to develop keratoses and skin cancers on the face backs of the hands or on the legs

Treatment —The skin can be protected from ultra violet irradiation by a cream containing 15 per cent of para aminobenzoic acid, 10 per cent salol or 5 per cent tannic acid in hydrous ointment or a particulate screen against ultra violet and visible rays can be provided by the compound paste of titanium dioxide Oily calamine liniment is necessary to soothe any severe reaction

DERMATITIS DUE TO RADIOACTIVITY

X rays and radium may cause acute changes in the skin, from one large exposure or several or chronic changes from repeated small exposures

ACUTE EFFECTS —Kienbock classified X ray burns as

First degree latent period 3 weeks no visible inflammation temporary shedding of hair

Second degree latent period 2 weeks redness and swelling of the skin lasting 1 to 2 weeks, falling of the hair

Third degree latent period 10 days redness superficial erosion and vesiculation parts restored to normal in 3 to 4 weeks

Fourth degree latent period under a week necrosis with ulceration healing takes 6 weeks or longer

Treatment of X ray burns is similar to that of other burns

CHRONIC EFFECTS —These are similar to those of repeated and long continued over exposure to the sun There is atrophic scarring with pigmentation depigmentation and telangiectasia Keratoses develop and squamous carcinoma may be the final result

DERMATITIS DUE TO MECHANICAL CAUSES

Continuous pressure on the skin tends to cause pigmentation and atrophy

Intermittent pressure causes corns and callosities

The acute effects of friction include blistering and epidermolysis bullosa the more chronic ones lichenification and hyperkeratosis

Excessive wetting of the skin causes the epidermis to become sodden and prone to fungous and coccal infection Excessive dryness of the atrophic skin causes a condition resembling a dried out mud bank with irregular or rounded areas peeling at their margins and with shallow fissures between them (eczema craquele) or deep fissures perhaps with secondary infection

DERMATITIS ARTIFACTA

Hysterical personalities sometimes produce blisters and sores on the skin by physical or chemical means and in so doing gain the sympathy freedom from work and (sometimes) pecuniary gain that they so much desire Of these motives the desire for attention loving care and sympathy is the strongest The lesions may be produced by sharp instruments friction constricting bandages hot coins cigarette ends caustic liquids and in various other ways

Clinical Picture —The patient is usually a young woman Usually there is a trivial wound or burn which does not heal as soon as might be expected on the contrary it extends with blistering or sloughing ulceration The lesions are bizarre discoid or linear sometimes with straight edges Hot coins cause round blisters cigarette ends cause small sloughing ulcers and caustic liquids cause linear discolourations dermatitis or sloughing often with a gravitational trickle where the caustic has flowed over the surface The lesions are always at sites easily reached by the right hand in right handed persons and at sites easily reached by the left hand in left handed persons the face breasts forearms and hands are favourite sites

The patient shows the belle indifference of the hysteric and examination reveals Charcot s triad of anæsthesia of the cornea and pharynx with suggestion anæsthesia of the skin perhaps in glove and stocking distribution

Hysteria cutis is also seen in other guises When compensation claims remain unsettled occupational dermatitis may continue as lichenified dermatitis long after the patient has been removed from the irritant This occurs particularly at the bends of the elbows in what may be called maintained dermatitis

In several other skin reactions particularly pompholyx eczematous dermatoses pruritus vulvæ infective dermatitis and psoriasis the persistence of the dermatosis or its exacerbation often seems to serve the purpose of enabling the patient to avoid some repugnant task or action and to receive care and attention The psychodermatological mechanisms of these conditions has not yet been explained

Treatment of all these hysterical reactions is extremely difficult It is one thing to understand the psychological mechanism but quite another to help the patient towards a better and more positive attitude to life It is useless to accuse the patient it will be indignantly denied A reasonable level of self esteem must be maintained Often the physician has to be satisfied with relief of the current manifestation by a modicum of sympathetic care and occlusive dressings knowing very well that the hysterical personality persists and will continue to react in this fashion to sundry future life situations Care should be given to finding suitable occupation, when work shyness is a factor The home conditions should be investigated and an attempt made to modify any unsuitable attitude of relations

DERMATITIS DUE TO CHEMICAL SUBSTANCES

Chemical substances may come into contact with the skin in gaseous liquid particulate or solid form and in so doing may cause dermatitis Two types of contact dermatitis are recognised

(1) DERMATITIS DUE TO PRIMARY IRRITANTS —These are substances that cause dermatitis in everyone if they are applied to the skin in sufficient concentration and for sufficient time They cause physio chemical alterations in the structure of the skin and act in various ways mechanical physical or chemical They may abrade the surface destroy keratin, abstract fat or mix with skin fat macerate or desiccate precipitate protein, oxidise or reduce hydrolyse form toxic nitro derivatives or stimulate keratin formation Primary irritants include inorganic acids and alkalis certain inorganic elements and salts organic acids solvents, essential oils certain dyes and tar and petroleum products

(2) DERMATITIS DUE TO SENSITISERS —These are substances which provoke dermatitis only in a few hypersensitive persons They consist mainly of complex organic chemicals, certain vegetable and animal products and a few inorganic chemicals which are able to take on sensitising properties when they are combined with protein They include plants dyes developers rubber accelerators and antioxidants soaps insecticides cosmetics oils, resins coal tar derivatives and explosives Certain chemicals and plants have a photo sensitising effect on the skin for example tar eosin, acriflavine sulphonamides and various plants including wild parsnips figs rue and many others Some substances can act both as primary irritants and as sensitisers For example soap has a primary irritant effect from its alkalinity and may have sensitising potentialities from the fatty acid part of its molecule Traces of chromium in cement may be responsible for sensitisation dermatitis from contact with this substance Bacteria fungi and parasites may cause or complicate occupational dermatitis

Ætiology and Pathology —*Predisposing causes of dermatitis* —Race complexion sex and age all modify the tendency to dermatitis White races are on the whole, more susceptible than dark races and blondes more than brunettes Women are more susceptible than men and children and the aged are more susceptible than young or middle aged adults But there are exceptions to these generalisations Sweating may leach out irritants from solids touched hairiness may carry with it some follicular vulnerability and although a greasy skin enables a person better to withstand contact with degreasing agents it also may expose him to greater peril from irritants that are miscible with skin fat Seasonal effects of sweating in the summer and chapping in the winter may be important An inherited susceptibility lack of cleanliness or reckless methods of cleaning up after work fatigue emotional instability or an anxious obsessional temperament and malnutrition may all play a part

Precipitating causes —The primary irritants most commonly responsible include soda and alkaline soaps cement and lime paraffin oil, petrol, diesel oil and turpentine

or turpentine substitutes lubricating cooling and cutting oils glue formalin phenol ultra violet or X irradiation or friction from gritty particles The sensitisers are many and include medicaments such as sulphonamides benzocaine penicillin flavine streptomycin formalin Lysol Dettol and adhesive dressings plants particularly Primula obconica chrysanthemums and many others teak ebony and other woods cosmetics including paraphenylenediamine hair dye eosin in lipsticks nail varnish bergamot oil and orris root powder clothes and jewellery including dyed furs wool and rubber chromium and nickel plating occupational hazards involving work with mercury chromium or nickel dyes and explosives flour improvers rubber antioxidants and very many others Occupations with more than average dermatitis *hazards include bakers carpenters cleaners dentists doctors dustmen dyers florists* french polishers garage hands gardeners housewives labourers machine hands miners nurses painters photographers platers rubber workers and tar workers

The development of dermatitis from primary irritants depends *inter alia* on the possession of skin secretions with poor alkali neutralising properties on some degree of xeroderma with insufficient sebum production to replace that removed by fat solvents and emulsifiers and on thinness of the horny layer

The cause of eczematous eruptions is the sensitisation of the epidermal cells to a continuously or repeatedly encountered agent It is possible that a heightened excitability of the nervous system as a whole (of which the skin is an end organ) is one important factor Sufferers from eczematous eruptions often show emotional lability which is more marked during exacerbations of the dermatosis and outbreaks may coincide with events causing emotional conflict

The mechanism of spread of eczematous sensitisation is far from settled There is some evidence that the lymphocytes convey antibodies to remote areas of the skin The manner of spread of eczematous processes also suggests nerve transmission as being partly responsible Sensitisation often spreads at first locally and then to a similar site on the opposite limb and to the comparable situation on the other two limbs before becoming generalised Examples of this include eczema of one leg spreading to the other and then to the forearms and ringworm of the feet with its manual mycide eruption

The incubation period from the first application of a substance to the development of sensitisation is variable and often indeterminable Flavine and sulphonamides may sensitise after 4 days penicillin after 8 to 10 days and some other substances after a longer interval Traumatic breaks in the continuity of the surface of the epidermis are most important The prickle cells of the Malpighian layer are normally protected from external noxæ by an intact horny layer and they react violently if they are exposed to primary irritants or to sensitising substances

In the acute stage there is spongiosis (intercellular and intracellular œdema) in the prickle cell layer causing microscopic or macroscopic vesicles and a variable degree of disintegration of the epidermis In the dermis a lymphocytic infiltrate surrounds the dilated vessels the sweat glands and the pilosebaceous follicles In the subacute and chronic forms there is parakeratosis (nucleated horn cells) acanthosis and a chronic inflammatory infiltrate in the dermis

The histopathology of dermatitis due to primary irritants differs from that of sensitisation dermatitis in that the infiltrate is more polymorphonuclear in the former and lymphocytic in the latter

Clinical Picture—In the most acute forms due to caustics there is destruction of the epidermis before an inflammatory reaction can develop In less acute forms there is smarting redness and swelling going on to vesiculation and blistering and a raw surface In subacute forms there is papulo vesiculation with abnormal scaling Milder and chronic forms present as redness and pathological scaling with lichenification increase of pigmentation and a tendency to fissuring

The reaction usually remains localised to the site of contact, sometimes with an

overlap of up to 0 5 cm apparently from a local reflex but if the irritant or sensitiser is in liquid or semisolid form, as often applies with contact medicaments the dermatitis tends to spread up to and just beyond the limits of each application If the irritant or sensitiser is miscible with sebum, the reaction may be mainly follicular and discrete follicular papules may develop beyond the zone of confluent dermatitis

Dermatitis varies in appearance according to the stage at which it is seen Erythema papulation or vesiculation predominate in the earlier stages later according to the degree of secondary infection or of rubbing and scratching it may go on to pustulation with moist infected scabs on an exuding surface or to lichenification and blood scabbing If neither complication develops resolution follows on the moist exuding surface by serous scabbing decreasingly coarse scaling diminution of redness and a return to the original state If at any stage a further contact with the causal agent takes place the whole process may recur

Course and Prognosis—This depends on the discovery of the cause and the possibilities of its subsequent avoidance Sometimes a trade irritant can be replaced by something harmless sometimes a process can be modified so as to lessen the exposure of the workman, sometimes protective clothing better ventilation and washing facilities are all that are needed 'Hardening by continuous re exposure is not likely to be successful With some specific sensitisers (for example streptomycin) desensitisation can be carried out, with others there may be a group sensitivity to chemically similar substances (for example sulphonamides flavine benzocaine paraphenylenediamine) or there may be a nonspecific broadening of sensitivity to many substances probably accompanied by increased emotional lability In this last form the prognosis is poor the causes often being undiscoverable

Diagnosis of primary irritant and sensitisation dermatitis on the face has to be made from solar dermatitis facial prurigo urticaria infective dermatitis and erysipelas on the body from ringworm seborrhœic dermatitis pityriasis rosea lichen planus psoriasis and parapsoriasis on the hands from nummular eczema mycides erythema multiforme and psychogenic pompholyx

Solar dermatitis affects the forehead and malar ridges contact dermatitis more characteristically affects the eyelids lips and neck, facial prurigo is accompanied by hay fever, asthma or flexural dermatitis urticaria is not accompanied by peeling erysipelas has a brawny spreading edge and there are constitutional symptoms on the body the other diseases and reactions are usually more circumscribed, on the hands nummular eczema affects the backs but adjoining areas escape entirely whereas with dermatitis the clefts are more typically affected and the eruption is more diffuse Psychogenic pompholyx is symmetrical whereas eczematous dermatitis of the hands may be asymmetrical At all sites frictional dermatoses (lichenification) have to be differentiated from spontaneous eruptions (eczema dermatitis)

The label contact (eczematous) dermatitis ' having been affixed on the basis of the morphology of the lesions the physician s more difficult task is to find the cause For this purpose it is necessary to know the ways in which sensitising substances may come in contact with the skin and the likelier causes of eczematous dermatoses affecting various parts of the body The problem is easier in dermatitis produced by primary irritants than when sensitisers are responsible The history is all important with possible seasonal fluctuations relief at week ends or on holiday and other significant evidence that the patient alone can supply Leading questions are necessary to uncover possible occupational causes including hobbies hygienic practices clothing cosmetics jewellery plants and other volatile agents day by day contacts and past treatments Sometimes the history can be supplemented by a diary of daily contacts kept by the patient after which patch tests can be performed with suspected sensitisers The distribution suggests the likely causes

On the scalp the likely causes include paraphenylenediamine hair dye permanent

waving solutions brilliantine and perfumes hair lacquers hat bands and occasionally medicaments On the face air borne and inadvertently hand transferred substances have to be considered also topical medicaments and cosmetics The eyelids are particularly affected by vapours and plant pollens thus formalin vapour primulæ chrysanthemums streptomycin are common causes as are also eye lotions drops and ointments and occasionally nail varnish and other hand transferred agents On the neck hair dyes fur collars and other dyed materials are suspect, also hand transferred irritants and dusts having a primary irritant action such as lime or cement Dusts also affect sites of pressure from clothing and within the socks as well as the hands Clothing when occasionally it is causal tends to affect the neck the axillary folds the belt line the buttocks hips and perineum the sock areas and the dorsa of the feet Nickel plated fittings and jewellery may affect many sites, including the neck lobes of ears mid line of back wrists and thighs

The pattern of contact dermatoses on the hands depends on the physical nature of the contactant solid particulate or liquid as well as on its chemical properties Liquids tend to affect the fronts of the wrists and the clefts of the fingers, powders have a more diffuse action inserting the hand into containers of powders or liquids may cause an eruption on the back of the hand and objects handled may occasionally cause eruptions at various sites depending on the type of grip

The accurate recognition of sensitisers depends to some extent on patch tests These are helpful if the results are interpreted correctly For success there should be adequate control suitable concentrations of the suspected sensitisers no patch testing with primary irritants inspection at 48 hours and reinspection at 3 to 5 days Contact eczematous responses (erythemato vesicular) must be differentiated from follicular obstructive effects (folliculo papulo pustular) and noted at the time of removal and from the trauma of removal of the adjoining adhesive (erythemato-folliculo papular occurring within a few minutes of removal) The conditions of patch testing and those in which the sensitiser is met in everyday life can never be identical (site sweating abrasions fissures friction etc) and allowance has to be made for this A positive patch test does not of necessity prove that the dermatosis was produced by this substance and a negative patch test does not completely rule out that the tested substance has been the cause of the original dermatitis Patch tests are best performed on the back of the chest The patient should not know which patch is which but suitable identification marks should be made on the adhesive dressings Patch testing should not be performed in the presence of active dermatitis and if the dermatitis has been severe patch testing should only be performed after complete clearance and with expert supervision the patient being instructed to remove the patches at once if a severe reaction occurs If this is not done an acute relapse may result at the sites of the original eruption

Treatment—This consists of prevention desensitisation when possible and symptomatic treatment

The essentials in the prevention of occupational dermatitis are selection of the most suitable workers their protection at work their periodic inspection and supervision to see that precautionary measures are conscientiously carried out and the provision of adequate washing facilities Selection includes rejection of hyperidrotic seborrhœic or xerodermatous individuals or those with prurigo tinea pedis or acne vulgaris as far as certain trade procedures are concerned Protection includes good ventilation abatement of humidity exhaust draughts suitable clothing and goggles and barrier creams which may have either water repellent or oil repellent effects and also emollient properties Inspection covers not only the working conditions and the proper use of protective appliances but also medical inspection of the workers for minor injuries and infections that may be the precursors of something more serious Washing facilities must be adequate and the worker must be discouraged from using paraffin petrol, scouring agents and other primary irritants for cleaning

the skin In some industries these are the cause of more sickness than the industrial hazards themselves

Desensitisation can occasionally be performed for example, in streptomycin cutaneous sensitivity by graduated intradermal injections This procedure is most valuable when the sensitivity interferes with a person's skilled occupation, but if the work is unskilled and there are opportunities for alternative employment it is better to remove the patient from the irritant than to attempt desensitisation, furthermore, hypersensitivity is often nonspecific and multiple sometimes only to similar chemical substances such as sulphonamides but in others to dissimilar substances and even to physical agents such as light

Attempts at hardening' by continuing to expose the worker to an occupational sensitiser are more likely to bring about ever increasing sensitivity, ending in generalised eczema than to succeed in enabling him to continue in the work

Local treatment in the acute phase consists of applications of oily calamine lotion with light dressings of butter muslin (which gets less entangled in the scales and crusts than does surgical gauze) held in place by cotton bandages The dressings are changed only once a day a bland vegetable oil or liquid paraffin being used gently to remove debris from the surface of the skin before another application of lotion is made For any infection that may develop soaks in 1 in 6000 solution of potassium permanganate are helpful, with applications of the appropriate antibiotic, depending on the cultural findings

As the condition gets less acute zinc or calamine cream or hydrous ointment may be used and when the eruption becomes scaly Lassar s paste or the ointment of wool alcohols are more useful Finally, if lichenification is tending to develop a 2 per cent tar paste makes a useful antipruritic application It is most unwise to use tar in the earlier stages and its use should be abandoned at once if there seems to be any tendency to the development of folliculitis At no stage should benzocaine anæsthetising substances be used in local applications as they have a great tendency in themselves to cause eczematous dermatitis Similarly, antihistamines are best avoided because eczematous dermatitis develops in about 3 per cent of cases in which they are used X-irradiation in fractional exposures is valuable in the chronic phase if the eruption persists in spite of nonexposure to the irritant

General treatment consists of rest to the body as a whole in widespread cases and to the affected part in local cases Sunlight heat and cold should be avoided Ample sedation to relieve the pruritus should be given In generalised cases due to sulphonamides flavine and other hepatotoxic substances the course may be shortened by intramuscular injections of a crude liver extract 4 ml daily

INFECTIVE (SEBORRHŒIC) DERMATITIS

This is one of the commonest and most important of skin diseases The term applies to many dermatoses differing in situation and pattern but in all of which there is a qualitative abnormality of the sebum The patient s skin is unduly susceptible to bacterial and fungous infection chemical and physical injury and emotional stress

Ætiology and Pathology—The triad of organisms found in seborrhœic dermatoses are the pityrosporon of Malassez (bottle bacillus) the acne bacillus and the *Staphylococcus saprophyticus* The organisms do not fulfil Koch s postulates in their relationship to seborrhœic conditions and they must be regarded as secondary invaders of the abnormal sebum follicles and horny layer

Histologically there is parakeratosis, hyperkeratosis and spongiosis (intra and intercellular œdema of the prickle cell layer) In the dermis, there is a lymphocytic infiltrate of moderate degree, with dilatation of the vessels

The seborrhœic individual is often obese and may indulge in fats and carbo hydrates to excess while taking insufficient exercise The diet is often deficient in foods containing protein and vitamins Drugs taken internally (for example sulphona mides) and various chemicals applied externally (for example flavine sulphonamides penicillin antihistamines and some occupational irritants) may provoke an infective outburst and emotional disturbances causing fear and loss of self esteem may have a similar effect

Clinical Types —There are three grades of intensity in infective dermatitis In the first and mildest there is a fine grey dry scaling showing on the scalp as dandruff or scurf (pityriasis simplex, seborrhœa sicca) without reddening of the underlying skin

In the second grade the scales are coarser and look and feel greasy (pityriasis steatoides) (This is due to a cellular infiltrate amongst the cells their fat content is not increased) The lesions may be solitary and pinhead sized grouped or con fluent and are found particularly where pilosebaceous follicles are most abundant

In the third grade there are moist red shiny exuding areas of skin with a sero purulent exudate and frank follicular pustules around The flexures are particularly affected and the horny layer of the opposing surfaces gets partly rubbed off and with the white sodden portions of epidermis remaining around a red shiny centre zone, gives the picture of intertriginous dermatitis Greasy crusts of seborrhœic impetigo may occur on the face and elsewhere Pyogenic staphylococci or hæmolytic strepto cocci may be found on culture or there may be a mixed infection with Gram-positive cocci and Gram negative fæcal contaminants

The sites commonly affected by infective dermatitis either alone or in combina tion are the scalp brows lashes eyelids conjunctivæ inner and outer canthi naso labial folds the vestibule of the nose postauricular folds over ears aural meati vermilion surface of lips angles of the mouth beard sweat grooves of centre of trunk submammary region axillæ navel pubis glans penis and coronal sulcus vulva genitocrural folds intergluteal cleft toe clefts and in discoid form on hairy areas of arms forearms thighs and legs as well as on the trunk

The possibility of an underlying infective dermatitis has to be considered in many cases of contact dermatitis and the converse also applies the diagnosis of infective dermatitis should not be made lightly without giving much thought to a possible contact cause for the attack

On the scalp there may be simple scurf (pityriasis simplex) on skin of normal colour or there may be profuse and widespread greasy scaling (pityriasis steatoides) on a reddened itchy skin the condition often extending a little on to the forehead as the corona seborrhœica The hair tends to fall more rapidly When the scalp becomes further infected with pathogenic cocci a condition of golden crusted and purulent seborrhœic impetigo arises

On the ears there may be a scaly and inflammatory condition of the meati perhaps with exudation or with folliculitis and perifolliculitis of the ceruminous glands giving rise to much pain and to varying degrees of meatal stenosis and deafness (meatitis) or the skin of the external ears may be inflamed (otitis externa) and scaling or exuding Above behind and beneath the ears the inflamed skin is very liable to crack and the painful fissures may form a portal of entry for streptococci causing streptococcal dermatitis or cellulitis (erysipelas) The ears are often contaminated with Gram negative fæcal organisms as well as with pathogenic cocci

The eyes may be affected in various ways—folliculitis of the brows or of the lashes (blepharitis) or styes inflammation of the skin and folds of the upper lids con junctivitis with chemosis and a slight sticky discharge or scaling and fissuring of the outer canthi.

The nose may have greasy scales and follicular plugs on the nostrils and at the nasolabial folds There may be a vestibular folliculitis

The vermilion surfaces of *the lips*, particularly the lower may show scaling and a tendency to crack (cheilitis exfoliativa) and angular stomatitis with fissuring is common

The beard area may be affected with a frank folliculitis (seborrhoeic sycosis) or there may be patchy or diffuse redness and exudate or scaling Occasionally impetigo is superimposed "Seborrhoeic" individuals are very susceptible to the haphazard and uncontrolled use of antibiotics and antiseptics on the skin, this is partly because they are very liable to become sensitised to topical agents, either the active component or the vehicle and partly because the use of antibiotics without previous culture and antibiotic sensitivity testing of the organisms grown often means that an unsuitable antibiotic is applied, with the result that the causal organisms thrive perhaps even being helped by the removal of competitors relatively harmless to the host

On the trunk, pityriasis simplex and steatoides are common in the mid line 'sweat grooves' In the obese intertriginous dermatitis may occur in all grades of severity in the axillary domes, under the breasts at the navel in the genitocrural folds and between the buttocks even under pendulous abdominal folds of fat Satellite follicular papulo pustules are grouped around the main lesions The coronal sulcus may be inflamed and balanitis supervenes (infective balano posthitis) *Folliculitis of the pubis* in varying degrees of intensity is present in the most intractable forms of this malady

Discoid or petaloid lesions of infective dermatitis may occur on the trunk and on the limbs particularly across the scapular region and on the extensor aspects of the limbs, even involving the backs of the hands or feet These lesions may be scaly sharply demarcated discs and ovals with a few discrete guttate papular lesions or in the more acute form there may be eczematous papulo vesicular discs going on to exudation and crusting (seborrhoeic, nummular or discoid eczema staphylococcide)

Intertriginous dermatitis between the toes makes an ideal medium for the growth of monilia and is a commoner cause of "foot rot than is pathogenic fungous infection in this region

In addition to all these patterns of infective dermatitis there are "seborrhoeides or 'eczematides conditions in which the use of one or other of various topical remedies sets off an explosive outburst of a papulo vesicular nature at first near the site of application later contralaterally and, finally in widespread fashion This condition is thought to be due to the development of sensitisation to bacterial or fungous products or the patient s own disintegrating epidermal cells or to the topical agent used (see autolytic eczema) It only occurs when there is profuse exudate or maceration at the primary site affected

Course and Prognosis are uncertain, owing to the constitutional factors concerned If the causal factors—dietetic drug contact emotional—can be altered or removed there is a reasonable prospect of success in cases where this is impossible for reasons of age environment or disposition the outlook is proportionately bad

Diagnosis —*On the scalp* the diagnosis is made from ringworm in children by examination for broken hairs microscopy and Wood's light examination Psoriasis of the scalp causes palpable discoid lesions with heavy scaling whereas in seborrhoeic dermatitis the lesions are impalpable except when impetiginised On the trunk the diagnosis is from pityriasis versicolor pityriasis rosea ringworm psoriasis and para psoriasis (*q v*)

Treatment —The general treatment consists of dietetic adjustment the withdrawal of any harmful contact or drug irritants and emotional adjustments where necessary or possible

The diet should be low in carbohydrates and fats and sufficient in protein and vitamin content The urine should be tested for albumin and sugar Alcohol chocolate, fried and spiced foods should be taken in strict moderation Vitamin B

complex and crude liver injections may help in cases with a history of dietetic im balance or with evidence of hepatotoxic effects from a drug or other cause

Local treatment for the scalp—a shampoo of 1 per cent cetrimide is most useful and this substance may be used for cleansing other affected areas of the skin

For pityriasis simplex a lotion such as that of salicylic acid and perchloride of mercury (N F) is useful rubbed in daily and gently with the finger tips

For pityriasis steatoides of the scalp the ointment of salicylic acid and sulphur (N F) is most useful but the strength should be reduced to 1 per cent when using it on children s scalps

For impetiginised lesions it is advisable to have a culture made and to use the best antibiotic according to the findings Until this result is to hand the use of 1 per cent cetrimide followed by zinc and copper lotion (D alibour water) as a local application should help

For infective dermatitis on the *trunk* the emulgent base in salicylic acid and sulphur ointment is likely to aggravate and recourse should be had to 1 per cent of sulphur or ichthammol or to 0 1 per cent of pyrogallol in calamine liniment or if there is more obvious infection Vioform cream (3 per cent) (Ciba) is often helpful

For *intertriginous dermatitis* antibiotics are best held in reserve until the cultural findings are known and recourse should be had to fungistatics such as magenta paint or to brilliant green 1 per cent in zinc paste or to Vioform cream When the moist phase has passed the patient should apply a bland dusting powder for example boric talc powder or salicylic acid dusting powders and keep the opposing skin surfaces apart with uplift breast supports and suitable clothing or gauze dressings

OTHER FORMS OF ECZEMATOUS DERMATITIS

The term eczema implies a boiling over of the skin and should be confined to spontaneous eruptions characterised clinically by papulo vesiculation and microscopically by spongiosis This definition excludes all primarily frictional dermatoses such as lichen simplex (neurodermatitis circumscripta) and disseminated neuroderma titis (atopic dermatitis)

A condition of uncertain status is exudative neurodermatitis in which extensive areas of exudation and crusting are present chiefly on the more distal parts of the limbs It is found in persons with hysterical traits and appears to be an exudative response to emotional stimuli particularly self pity

NUMMULAR ECZEMA

Nummular (discoid) eczema (infectious eczematoid dermatitis) is an outbreak of papulo vesicles often confined to the more hairy surfaces of the limbs particularly the forearms and legs but sometimes becoming more generalised Sometimes dis crete shotty vesicles appear as well A chemical contactant cannot be incriminated and the malady is probably related more to sensitivity to skin resident organisms particularly *Staphylococcus saprophyticus* and monilia

Infectious eczematoid dermatitis is a disorder closely related to nummular eczema in which the discharge from an area of infective dermatitis produces a mixed eczema tous and infectious (impetiginous) reaction wherever it touches

Treatment —Nummular eczema responds best to nonsensitising bacteriostatic and fungistatic remedies such as chlortetracycline ointment chloramphenicol cream Vioform cream magenta paint or brilliant green in zinc paste Symptomatic treat ment should also be given to relieve depression if present by dextroamphetamine 5 mg in the morning and insomnia from itching by barbiturates or promethazine

hydrochloride in the evening In resistant forms a course of intravenous T A B 25 million, 50 million and 100 *million organisms at 5 to 7 days' intervals may bring* about a remission X irradiation in fractional doses is often effective

POMPHOLYX (DYSIDROSIS)

This is a vesicular eruption of the palms and of the palmar and lateral aspects of the digits and of the under surfaces of the feet It is often recurrent.

Ætiology and Pathology—This is a skin reaction which may be secondary to fungous infection of the feet (mycide) it may be a manifestation of eczematous dermatitis exogenous or endogenous, or it may be of psychogenic origin an hysterical phenomenon serving the purpose of preventing the sufferer from performing some task which is distasteful

Histologically there is spongiosis as in eczematous dermatitis elsewhere The vesicles remain intact owing to the thick horny layer above them There is no evidence of obstruction of the sweat ducts, except secondarily through pressure from the *adjacent vesicles but clinical* experience of the seasonal incidence and of aggravation by heat, exertion or anxiety suggests that some abnormality of the sweat apparatus (so far unexplained) plays a part in the pathogenesis

Clinical Picture—There are vesicles of uniform size, resembling frog spawn in the skin of the palms and fingers and on their lateral aspects The backs of the hands may be quite normal The feet may show a similar condition in a comparable distribution The affected areas do not sweat There is considerable itching until the fluid is either reabsorbed or discharged by rupture of the vesicles Coarse peeling follows and resolution may occur or the whole process may be repeated

Course and Prognosis—This depends on the cause whether it be fungous infection eczematous hypersensitivity or an hysterical personality The form due *to fungous infection does well when the infection is controlled* The other two forms tend to recur unless a sensitising substance can be found and subsequently avoided, or unless the patient can be brought into better adjustment with life situations

Diagnosis is from pustular psoriasis, erythema multiforme and tinea pedis The *former presents with golden yellow pustules from the beginning*, whereas in pompholyx the vesicles are skin coloured at first

In erythema multiforme there may be large bullæ and there is also erythema, which is absent in pompholyx

Tinea pedis presents with large bullæ in the roofs of which mycelial threads *may* be found on microscopy but the same foot may also have on it many *small vesicles* of pompholyx type (mycide) in which fungus cannot be found Tinea pedis is *often* asymmetrical its mycide symmetrical idiopathic eczematous and psychogenic pompholyx are symmetrical but contact eczematous dermatitis is often asymmetrical

Treatment is bland and supportive by Lassar's paste hydrous ointment or calamine lotion while the fungous infection is being controlled while irritants and sensitisers are being avoided or while the patient is receiving psychotherapy If infection becomes superimposed—and this often occurs with purulent blebs lymphangitis and lymphadenitis—the part should be elevated and kept at rest Soaks *for* 10 minutes in a 1 in 6000 solution of potassium permanganate are useful and sulphonamides or penicillin may have to be used systemically

In many patients it is necessary to give sedatives for example phenobarbitone in a dose sufficient to control itching and to provide sleep

AUTOLYTIC ECZEMA (ECZEMATIDE)

This is a widespread papulo vesicular eruption arising from absorption of products from an area of erosion or of ulceration The absorbed products may originate from

organisms on the skin or they may result from the breakdown of body cells The process is more likely to occur with the use of certain substances on the skin particularly sulphonamides flavine paraphenylenediamine benzocaine mercurials etc but it may even develop from the occlusion of a moist area by soft paraffin which suggests that the substances applied are not primarily responsible but that they hasten cellular disintegration or encourage infection Autolytic eczema typically arises from faulty treatment of ulcers or eczema (eczematide) on the legs but it also arises from over treatment of extensive abrasions second degree burns herpes simplex eczematous or infective dermatoses

Prevention and Treatment—This condition is preventable by avoidance of the use of powerful sensitising agents on the surface such as sulphonamides flavine picric acid mercurials and benzocaine also by not using occlusive soft paraffin dressings over moist areas

It is best treated by application of oily calamine the use of sedatives and intramuscular crude liver extract injections

ENDOGENOUS ECZEMA

A widespread papulo vesicular eruption for which no immediate contact cause can be found Sometimes the epidermal sensitisation has arisen from the administration of a drug (for example sulphonamide) previously used topically but often the most careful history fails to elicit any cause in the form of a focus of infection drug food or metabolic disorder Such patients are often tense over active obsessional personalities and this make up seems to be of ætiological significance

Treatment—Bed rest is advisable in the more severe forms Suspected foci of infection are treated and the patient is given a diet of high protein and vitamin content which is not water retaining The intake of fats and carbohydrates alcohol coffee and condiments is reduced Sedatives are given by mouth and bland local applications are used T A B injections are sometimes useful If the condition is believed to be an exudative neurodermatitis the patient should be encouraged to lead an active life and to discard feelings of self pity if as often happens these are present Dextro amphetamine 5 mg after breakfast is a useful remedy for this type of patient

INFANTILE ECZEMA

The term covers infective eczema of infants and the earliest papulo squamous stages of the condition called Besnier s prurigo later in life Both forms may coexist

In the infective variety there is greasy scaling of the scalp and sometimes of the face chest and flexures The child is usually overweight

In the pruriginous form there is a widespread erythemato papulo squamous rash with exudation and crusting affecting particularly the face and parts of the limbs and body most accessible to the infant s efforts at scratching and rubbing that is the shoulders elbows wrists and hands knees legs and feet The trunk is only slightly affected with a blotchy erythemato papular eruption

Ætiology—Infantile eczema is in part due to inherited abnormalities in part to an unfavourable emotional environment and in part to faulty feeding practices It is seldom due to allergy to foodstuffs

In the infective form an excess of fat or carbohydrate in the diet is often an important factor This may occur because the child is weaned at an early age on to a full cream milk because of failure of lactation It may also occur at or about 6 months because the child is given excess of cereal foods The skin as a result becomes

susceptible to infection by organisms resident on the skin (*monilia* and *Staphylococcus saprophyticus*)

In the rare allergic form milk (lactalbumin) or cereal products are usually responsible

The more common pruriginous form (atopic eczema) is in part due to an inherited predisposition and in part due to an unsatisfactory mother child relationship in which an emotionally labile mother who is unable to give the child the steady and unselfish affection it needs clashes with a child of higher than average intelligence and peculiarly prone to itching and frenzied rubbing and scratching whenever deprived of pleasurable activities or of affection Pruriginous eczema sometimes complicates xeroderma

Course and Prognosis—The infective type tends to clear up with suitable dietetic adjustments and local treatments, but it may relapse

The allergic form responds to the withdrawal of the proven allergen provided this is the only cause

The pruriginous form tends to get better at 1½ to 3 years when the child can do more for itself in exploration of its environment There is however, often a recrudescence at or about puberty this time with a preponderance of facial and flexural involvement (Besnier's prurigo)

Diagnosis—The affixment of the label 'eczema' offers no difficulty the problem is to apportion blame to inheritance environment diet and infection and this depends on a careful review of the history and signs

Treatment—In the infective form the protein vitamin and mineral content of the diet should be rendered adequate but fats and carbohydrates should be reduced Thus egg yolk bone broth, sheep's brains, tripe and pounded fish may be recommended with spinach puree and other sieved vegetables, cereals full cream milks or addition of sugar are best avoided half cream milk being offered instead

Local treatment depends on the degree of infection If this is severe the most suitable antibiotic should be applied If milder, the skin may be cleaned with a 1 per cent solution of cetrimide, and 1 per cent of salicylic acid and of sulphur in an emulgent base applied Later, oily calamine lotion can be substituted

The child should be cleaned as a routine with olive oil, and a superfatted soap used when necessary

The diagnosis of allergic eczema is made by elimination diets Cow's milk is first omitted If there is improvement lactalbumin of milk is suspected as the cause If there is no improvement cow's milk is given alone for 24 hours and then one item is added each day until any aggravating factor or factors are found Those are then omitted from the diet If cow's milk is the cause goat's milk can be substituted or a lactalbumin free product (for example Allergilac)

Pruriginous eczema depends for its control on adjustments in the mother child relationship as well as on all the physician can do by bland local applications restraining appliances and sedatives The mother and all around the child should be encouraged to generate a calm and unselfishly affectionate atmosphere The child should be kept fully occupied with suitable toys on which he can relieve his aggressive urges but in infancy it may be necessary to tie the limbs with broad crepe bandages to the sides and foot of the bed providing adequate protection to the skin where they are applied so that damage cannot occur It is only in this way, and with sedation pushed to the limit that the child can be kept from rubbing and scratching its face and limbs until they are raw Eczematous children tolerate sedatives such as phenobarbitone in higher doses than the more normal child, and a dose of gr ¼, three or four times a day for a child 12 months old is nothing unusual In milder cases the elixir of Benadryl or of promethazine hydrochloride or a chloral and potassium bromide mixture may be sufficient

Local applications should be bland and free from sensitising properties The

watery or the oily calamine lotion zinc cream zinc paste or hydrous ointment are all useful at times Hydrocortisone ointment 1 to 2 5 per cent has been reported to be effective

Where treatment is not proving successful at home a period in hospital is sometimes of great value but this has to be balanced against the risk of these children getting widespread pyogenic or virus skin infections to which they may succumb

ERYTHEMA INFANTUM (NAPKIN ERUPTION)

Erythema of the napkin area may be due to infection or to chemical irritation The *infective form* involves the depths of the folds of skin It may be a part of pemphigus neonatorum The chemical irritative form affects the summits of the folds of skin buttocks thighs etc Sometimes the cause is urea splitting organisms in the infant s fæces The resultant ammoniacal urine causes a contact dermatitis (Jacquet s erythema) In other cases excesses of fat or sugar in the infant s diet may result in stools that irritate the skin Occasionally insufficient rinsing of the napkins after they have been washed is responsible for an alkaline or detergent dermatitis

Treatment —*In the infective form cleansing with 1 per cent cetrimide and the* application of an inert dusting powder is often sufficient or the appropriate antibiotic can be applied after cultural examination

In the chemical irritant form treatment depends on the cause but further aggravation must be prevented by the application of zinc and castor oil cream to the infant s buttocks

Dietetic adjustments may be necessary or greater care in rinsing the napkins In Jacquet s erythema soaking the napkins in a quaternary ammonium compound or in saturated boric acid solution before use is effective The napkins should be rinsed thoroughly after these procedures before use

HYPOSTATIC ECZEMA AND ULCERS ON THE LEGS

Defective venous return of blood from the legs leads to a gradual deterioration of the vitality of the skin of the lower parts of the calves and ankles resulting in the various clinical conditions known as hypostatic eczema Minor wounds of the legs are always apt to take longer to heal than similar wounds on the upper limbs even in healthy youths This tendency to poor healing is accentuated if there is any deficiency of the veins either through incompetent valves or deep thrombosis each of which may be responsible for the development of varicosities but varicosities in themselves are not the cause of eczematous and ulcerative changes eczematous changes are due in the first place to chronic congestion and anoxæmia while ulceration is due to superficial venous thrombosis causing a focal necrosis in the dermis

The congested anoxic legs tend to itch scratches or other minor injuries do not heal but tend to exude Mild secondary infection causes an aggravation of the condition and many patients treat themselves not by rest with elevation of the limbs or by suitable supports to the legs but by local applications one or other of which in time sets off a contact eczematous reaction Further misguided treatment with antiseptics and other potential sensitisers results in the picture of chronic exuding eczema of the legs

With appropriate treatment the exudation stops and is replaced by coarse peeling from the swollen reddened skin Gradually the peeling becomes less conspicuous and provided lichenification does not develop ultimately it stops the leg being left pigmented and possibly somewhat indurated but dry

Ulcers may develop from abrasions scratch marks cuts or bruises on the leg

The skin below and behind the medial malleolus is a specially vulnerable area no doubt in part because there may be a downward back pressure from the pumping action of the calf muscles and in part from the poor support and lack of rest supplied by the underlying tendons Stasis and local œdema are the most important factors in the non healing of ulcers of the leg and secondary infection is usually a minor feature, but sometimes healing is prevented by a heavy mixed infection of cocci *Ps pyocyanea* and *Proteus*, or streptococci may gain entry and cause cellulitis followed by chronic solid œdema of the part (*elephantiasis nostras*)

Diagnosis —Most ulcers on the legs are hypostatic and related to thromboses varicosities and chilblains but some are arteriosclerotic as shown by absence of pulsation in the dorsalis pedis artery and radiographic evidence of calcification This may occur with or without diabetes

Gummatous ulcers are often higher up the calf serpiginous in outline, ham coloured and appear as if punched out Lupus vulgaris, sporotrichosis and halogen granulomata can all cause leg ulcers

Rodent ulcers occasionally form on the legs and nodes of Hodgkin's disease or some other reticulosis may break down in that situation

Pseudoepitheliomatous hyperplasia is a warty condition clinically and histologically resembling carcinoma but due to over treatment of an ulcer with sensitising local applications It clears up when the irritant is withdrawn

Ecthymatous ulcers are moist, with dirty sloughs and no signs of granulations

Treatment *of hypostatic eczema* is supportive by suitable elastic hose or bandages with bland non absorbable local applications, for example calamine liniment

If the exudation persists in spite of this an ointment of 12½ per cent of solution of aluminium acetate with 37½ per cent of zinc paste and 50 per cent of lanolin may prove effective In the scaling, lichenified stage X irradiation in fractional exposures may help Unna s gelatin paste or zinc paste bandages are u eful in the subacute or chronic stages but adhesive bandages should not be used The patient needs to wear a support to the leg indefinitely or in suitable cases provided the deep veins are patent the varicose veins may be given surgical attention by injections and ligations

Treatment of hypostatic ulcers aims at reducing local œdema Tulle-gras is applied to the ulcerated area with an overlying gauze orthopædic felt or sponge rubber pad covering the ulcer and the skin around the whole leg being firmly bound with an elastic bandage The patient is encouraged to take exercise and is warned about the bad effects of prolonged standing Massage to the surrounds of the ulcer and to the limb as a whole is helpful Any infective element is controlled by the appropriate antibiotic Any excessive granulations are reduced by a silver nitrate pencil

Surgical treatment of any varicose veins is carried out in selected cases

COCCAL INFECTIONS

In health the intact skin is able to resist invasion by organisms falling upon its surface Infections result either from breaks in the surface of the skin or from some abnormality of its acid mantle This mantle is formed by the continuous slow extrusion of sebum from the sebaceous glands through the pilo sebaceous orifices and the emulsification and spread of the sebum over the surface by means of the sweat

Dehydration of the surface is another important factor in the prevention of infections *Sweat retained on the surface* particularly in body folds provides ideally moist warm conditions for bacterial growth, and sweat when decomposing by bacterial growth becomes alkaline, which further encourages the bacteria

Coccal infections of the skin are encouraged by anything that causes breaks in the surface such as clumsy hair cutting or shaving rough clothing scratching or

dermatitis leading to fissuring also of importance are the qualitative and quantitative abnormalities of the sebum which occur in seborrhœic dermatitis and xeroderma and excessive sweating particularly in obesity when skin surfaces chafe and rub off the superficial epidermal cells

Skin infections are more common with diabetes mellitus in toxic states such as uræmia in states of nutritional deficiency and in blood diseases for example leukæmia

Before considering infections at various anatomical situations in the skin it is well to remember that in all cases of severe or widespread coccal infection a cause must be looked for locally (infestations, itchy dermatoses) and generally (diabetes uræmia leukæmia anxiety neurosis etc) Attention must also be paid to potential carrier sites of staphylococcal infection especially the hairy vestibule of the nose

IMPETIGO VULGARIS (IMPETIGO CONTAGIOSA)

Impetigo is a coccal infection of the epidermis sometimes involving the ostia of the pilosebaceous follicles (follicular impetigo) or of the sweat ducts (infected miliaria rubra Bockhart s impetigo)

Ætiology and Pathology—Impetigo vulgaris is usually a disease of children but may occur in adults with the seborrhœic diathesis (seborrhœic impetigo) It usually follows some break in the skin s surface caused by insect bites scratching or the rupturing of herpetic bullæ Purulent discharges from the nose ears or eyes are often responsible or the infection may be transferred to the face and other exposed parts from a paronychial whitlow Nasal diphtheria may be complicated by impetigo

Clinical Picture—The lesions of impetigo consist of golden or dirty greenish grey stuck on crusts discoid polycyclic or annular scattered over the face scalp or limbs amongst areas of normal skin Occasionally there are intact bullæ containing thin pus Similar lesions may be present in the nostrils It is not possible on clinical grounds alone firmly to differentiate between staphylococcal and streptococcal impetigo Although streptococci may be present in the early stages *Staphylococcus pyogenes* usually predominates in any culture that is made and is often grown in pure culture

At the angles of the nose or mouth and behind the ears fissures may form with exuding red sodden or crusted skin nearby

Course and Prognosis—Without treatment impetigo may continue for several weeks In every case the precipitating cause must be dealt with for example pediculosis otorrhœa rhinorrhœa or scabies because once this is under control the elimination of the coccal infection is a simpler matter Use of the appropriate antibiotic then leads to clearance in 3 to 7 days Occasionally impetigo is complicated by nephritis Impetigo should be investigated epidemiologically in order to control the outbreak in a family or school Contacts should be examined for banal lesions septic fissures running noses etc

Diagnosis—It is important to differentiate impetigo from herpes simplex and from eczematous dermatitis on the face whether infected or not

In herpes simplex the vesicles often remain intact for a while they are grouped and contain clear fluid Impetigo may originate from infection of ruptured herpes vesicles but eczematous dermatitis may also begin from the faulty treatment of herpes simplex with antiseptics or antibiotics

In eczematous dermatitis the lesions at first spread in continuity from the site of application of the irritant but later they may erupt symmetrically in explosive fashion In impetigo the spread is more irregular and impetuous skipping areas of normal skin with the effect that individual lesions develop rapidly by peripheral spread at several sites of skin inoculation

Treatment—If pediculosis or scabies is present it should be dealt with first Any residual infection that persists may then receive attention

If an intensely itchy skin disease such as prurigo coexists, it should be controlled by suitable sedatives by mouth and the superimposed impetigo only treated for as long as is necessary before proceeding to suitable treatment of the underlying dermatosis

Ideally a culture should be made and the organisms tested for their susceptibility or resistance to various antibiotics, but with a short term disease such as impetigo the usual practice is to apply the antibiotic believed by the prescriber to be most effective Chloramphenicol, chlortetracycline (Aureomycin) and oxytetracycline (Terramycin) are all effective in many cases but, in common with penicillin they are unsuccessful in those infections due to resistant strains which are becoming more common

Antibiotics are far from being the *sine qua non* in the treatment of impetigo Simple desiccation may be quite effective, and for this purpose calamine lotion is effective with the addition of 0 1 per cent of mercuric chloride if desired Calamine liniment may also be used, or zinc paste with 2 per cent of salicylic acid (Lassar s paste) To the last named may be added 1 per cent of ammoniated mercury or of brilliant green

Loose crusts and intact bullæ should be removed before any remedies are applied For this purpose normal or slightly hypertonic saline may be used or a 1 per cent. solution of cetrimide which has the added advantage of its antiseptic properties

No antibiotic should be persisted with for more than 3 days if it is not giving satisfactory results Failure to respond implies resistant organisms and continuing the use of the antibiotic may lead either to a spread of infection or to the development of eczematous hypersensitivity Two per cent of silver nitrate in spirits of nitrous ether is useful as a paint for application to fissures

PEMPHIGUS NEONATORUM (IMPETIGO NEONATORUM)

This is a form of staphylococcal impetigo affecting newborn infants highly infectious and having a considerable mortality rate

Ætiology—The infection begins from an extraneous source for example a cutaneous or nasal infection or carrier state in a medical or nursing member of a maternity unit a visitor, a lay worker or one of the patients One attendant may infect several infants

Clinical Picture—Large bullæ containing thin pus cover the body surface and pink, shiny moist areas indicate where bullæ have ruptured The widespread severe and often fatal form of the condition resembles exfoliative dermatitis (dermatitis exfoliativa neonatorum of Ritter) It has recently been suggested, however that Ritter s disease is caused by the application of napkins which have previously been soaked in boric acid

Course and Prognosis—Premature and inadequately treated infants may succumb to the infection but as a rule patients respond to antibiotic therapy A careful search must be made for the primary source for carriers and possible conveyance by fomites As a precaution, all in attendance on newborn infants should wear efficient surgical masks

Diagnosis is from congenital syphilis in which the pemphigoid lesions occur on the palms and soles as well as elsewhere Other signs of congenital syphilis may be present including rhagades snuffling etc

Treatment is by the appropriate antibiotic locally also systemically if this seems advisable Good nursing is essential and protection of the child from chilling when dressings are being done

IMPETIGO PITYROIDES (PITYRIASIS ALBA)

This consists of scaly depigmented discs which occur on the faces of children The lesions are believed to be streptococcal and mildly infective, but drying winds

and the excessive use of soap seem to play an equally important part in their production

Treatment—The lesions usually respond to the application of weak ammoniated mercury ointment or to 2 per cent of solution of coal tar in Lassar's paste

PYOGENIC PARONYCHIA (see Diseases of the Nails)

ECTHYMA

This is a coccal infection originating from the surface and affecting the dermis leading to necrosis ulceration and scarring Trauma is an important predisposing factor

Clinical Picture—This malady is more common amongst under nourished ill-cared for children and amongst individuals of low intelligence than among clean and normally intelligent persons It usually affects the legs where one or several areas of dirty grey crusting may be seen with a purulent discharge and red surrounds Later the crusts become detached leaving shelving ulcers with an inflammatory rim and a sero purulent base There may be regional lymphadenopathy Ecthyma may also occur in adults suffering from pediculosis or from infection of traumatised legs (for example desert sores)

Course and Prognosis—If untreated the condition may persist indefinitely and it may spread as impetigo or furunculosis on other parts of the body

Diagnosis—An ecthymatous syphilide must be excluded

Treatment—Having excluded any parasitic infestation attention is directed to any malnutrition and uncleanliness that may exist

For local treatment cleansing with 1 per cent cetrimide is indicated followed by application of the antibiotic most suitable according to the cultural findings This is likely to prove effective more rapidly than nonspecific remedies such as eusol compresses or a lotion of sodium hypochlorite Desiccating measures may also be employed The nails should be kept closely trimmed and attention paid to any infective foci in the nostrils or paronychial folds

FOLLICULITIS

Coccogenic folliculitis is one form of sycosis barbæ (folliculitis profunda) the other being mycotic folliculitis Folliculitis may also be superficial (ostio folliculitis Bockhart's impetigo)

FOLLICULITIS BARBÆ

Clinical Picture—Folliculitis barbæ is a chronic staphylococcal inflammation of the depths of the hair follicles in the beard region Folliculitis profunda may also occur at other sites for example the nucha and the pubis

Discrete follicular papules and pustules are present and from them hairs protrude The lesions may be grouped or diffusely confluent all over the beard area Tender nodules may form In long standing cases due to antibiotic resistant strains the efforts at cure with sundry medicaments may end in a mixed condition of folliculitis and dermatitis presenting as diffuse redness and exudation or scaling interspersed with follicular pustules

Ætiology and Pathology—Shaving trauma and staphylococcal infection

Course and Prognosis—The progress of folliculitis depends on the susceptibility or resistance of the causal organisms to antibiotics In the majority relief can be obtained with one antibiotic or another but it is always wise to have a culture made and the antibiotic sensitivity of the organisms investigated before starting treatment especially as antibiotic resistant strains of staphylococci are becoming more

common Furthermore, many individuals with folliculitis show other signs of the "seborrhœic" diathesis which indicates that they are susceptible to infection of the skin Sycosis in them may present with less frankly purulent lesions the organisms responsible being less potent strains of *Staphylococcus aureus* or even *Staphylococcus albus* and not the coagulase positive *Staphylococcus aureus* usually met in folliculitis

If folliculitis relapses in seborrhœic individuals it may be because of invasion by a different strain of organisms with different antibiotic sensitivities For this reason, it is advisable to repeat the culture and antibiotic sensitivity tests in any relapse

In every case of staphylococcal folliculitis it is essential also to take a swab and to culture the organisms from the nasal vestibule and to treat this carrier site of staphylococci with the appropriate antibiotic It is not necessarily true that the organisms cultured from lesions on the skin are alone responsible for the development of that lesion A coccal infection may be superimposed on a syphilide, and organisms such as *Staphylococcus saprophyticus* and Gram negative organisms of the coli group *Ps pyocyanea* or *Proteus* may be secondary invaders of devitalised tissue Fæcal *contaminants do, however, seem to play a significant role in some cases*

Diagnosis has to be made from impetigo mycotic folliculitis chemical folliculitis foreign body reactions due to ingrowing hairs infected acne and syphilis In impetigo the lesions are superficial and not necessarily follicular In mycotic sycosis the patient gives a history of contact with cattle the lesions are much more acute and œdematous and hairs can easily be pulled out from the follicles fungus spores may be found (often with some difficulty) on removing infected hairs

Chemical folliculitis is usually due to over treatment or to faulty treatment of a non infective dermatosis of the beard area with antibiotics or antiseptics It is recognised by the presence of diffuse dermatitis and much serous exudate as well as folliculitis

Foreign body reactions due to ingrowing hairs are most common in coloured men with curly hair running in every direction which, on shaving tends to become embedded in the skin This especially occurs on the sides of the neck under the chin line but may also occur on the face It occasionally occurs in white men particularly those who shave very closely against the grain Embedded hairs are visible on inspection with a hand lens and their free ends can be extracted with a needle Culture in such a case usually grows saprophytic organisms or coliforms

Infected acne occurs in the skin immediately adjoining the beard area but may coexist with folliculitis barbæ The presence of comedones is an essential feature in the diagnosis of acne

Syphilis may in the secondary stage present with pustulation and frambœsiform crusts at the cleft of the chin Its presence should be suspected from any atypicality of the lesions and any signs of syphilis elsewhere Lupoid sycosis is differentiated from lupus vulgaris by the presence of atrophic scarring with occasional pustules and by the absence of apple jelly nodules

Treatment consists of the application of the appropriate antibiotic to the lesions and if necessary to the nostrils three or four times a day This treatment should be persevered with for a fortnight after apparent clinical cure even after that interval, *relapses are common in seborrhœic* individuals With penicillin a lotion is often more effective than a cream and less likely to sensitise the skin but it may prove too drying With chloramphenicol chlortetracycline and oxytetracycline ointments *or creams are usually effective* and they are pleasant to use

Other applications which may prove relatively effective include quinolor ointment Vioform cream and ammoniated mercury but they all have in varying degrees *a tendency to sensitise the skin* Zinc and copper lotion (D alibour water) is useful as an after shave lotion In very severe or resistant forms of folliculitis barbæ it may be advisable for the patient to use an electric razor Growing a beard is a satis

factory alternative The use of X rays in folliculitis barbæ is contraindicated both in fractional and epilatory doses

OSTIO FOLLICULITIS (BOCKHART S IMPETIGO)

Ostio folliculitis is a staphylococcal infection of the orifices of the follicles

Ætiology —Ostio folliculitis is caused by stimulation of the epidermis by oil adhesive plasters or other surface irritants It is often a complicating feature of prickly heat (*miliaria rubra*)

Clinical Picture —Discrete superficial pustules are present at the orifices of hair follicles Hairs penetrate the pustules On rupture superficial erosions are left The lesions are often grouped but sometimes extensive There is often an associated keratosis follicularis or acne because the irritants causing the folliculitis also stimulate epithelial proliferation at the ostia The sites usually affected are the forearms and thighs

Course and Prognosis —This depends on the future avoidance as far as possible of contact with irritants such as oil adhesive plaster powerful degreasers and de hydrators The worker should be given facilities to wash parts exposed to oil im mediately after work is finished he should be discouraged from postponing washing until he gets home perhaps after a considerable journey The condition is then likely to clear

Treatment —Parasitic infestation must be excluded A culture should be made and the appropriate antibiotic used Vioform cream is sometimes effective and D alibour water is useful followed by lead and calamine lotion

PILI INCARNATI (see Folliculitis Barbæ)

Treatment —The only treatment of value for this relatively mild but annoying condition is the avoidance of close shaving particularly with the skin under tension The shaver should aim at the sort of result obtained by one shave with the grain Electric razors are not necessarily an advantage

BOILS AND CARBUNCLES

A boil (furuncle) is a staphylococcal infection of a sebaceous gland proceeding to a perifollicular abscess sloughing of the hair papilla and of the pilosebaceous follicle and its replacement by scar tissue

Furunculosis is a condition of multiple localised or widespread boils A carbuncle is a localised group of boils which by their mutual pressure cause sloughing of exten sive areas of skin and subcutaneous tissue with much constitutional disturbance

Ætiology and Pathology —Boils are usually due to some local breakdown in the skin s protective mechanism Carbuncles are usually due to some general lower ing of resistance Thus boils may be secondary to scratch damage in an itchy skin condition whether it be parasitic infestation dermatitis or prurigo or they may result from local damage arising from shaving or haircutting rough clothing oil or dirt A carrier site of staphylococci in the nose is often the source from which the skin is inoculated and furunculosis may set a problem in domestic epidemiology in which the sharing of face flannels towels etc may prove to be responsible for the spread of infection within the family In every case of furunculosis and more espec ially with carbuncles attention should be directed to the possible presence of diabetes renal disease leukæmia or nutritional deficiency either of insufficiency or of imbalance

Clinical Picture —A boil begins as a painful red nodule which enlarges and becomes hard and tender At its centre a small papule or papulo pustule is visible penetrated by a hair Induration and pain cause difficulty in moving the affected

part After 36 to 48 hours the centre softens, a small scab or slough detaches and a purulent discharge begins In another 36 to 48 hours the 'core' or pilosebaceous slough is extruded the purulent discharge and induration lessens and the boil heals with a varying amount of scar formation

A carbuncle begins with greater constitutional disturbance Instead of a nodule there is a brawny plateau in which several follicular pustules can be seen The mass enlarges and a shelving induration with œdema extends for some way around Softening and liquefaction of the mass may (in patients treated by local application only) take days or even a week or two, but sooner or later a large slough forms and is gradually detached or many points of suppuration develop, with subsequent extensive scarring Smaller boils and follicular pustules around the main lesion often form as a result of auto inoculation

Course and Prognosis —These depend on the cause and the ease or difficulty of its removal With itching due to infestations, it is easy with itching due to emotional conflict it may be extremely difficult A carbuncle in a debilitated patient is a serious and sometimes fatal condition

Diagnosis —A boil or carbuncle has to be diagnosed from a malignant pustule (anthrax) In the latter, the onset is more rapid and the constitutional symptoms are more marked while the history of exposure to wool or hides makes the diagnosis likely Culture or even a direct smear will usually reveal the bacilli but treatment should be started on clinical grounds alone, without awaiting cultural confirmation

The primary tuberculous complex resembles an indolent boil but the youth of the sufferer, a history of contact, the lymphadenopathy draining the site of inoculation and the resistance to antistaphylococcal measures should arouse suspicion

Treatment —In every case the cause should be looked for and treated if possible Glycosuria or albuminuria malnutrition or leukæmia should all be excluded If itching preceded the boils this should be investigated Occupational hazards unsuitable clothing and faulty hygiene practices should receive attention

Severe boils and carbuncles are best dealt with by systemic penicillin or some other suitable antibiotic depending on organismal sensitivity tests Smaller lesions are better treated by local remedies Penicillin injections are a passive treatment having no value for stimulating the reactivity of the host in fact the converse sometimes applies penicillin injections being followed on cessation by a crop of further boils of even greater severity For this reason it is a mistake to give penicillin at once without first investigating the cause of the infection and the susceptibility of the organisms to antibiotics Vaccines staphylococcal toxoid manganese injections and tin by mouth have a reputation for relieving furunculosis but their effects are most uncertain

Local treatment should aim at resolution of the lesions with minimal discomfort and with the avoidance of further contamination of the skin by the pus coming from the boils Softening or maceration of the skin must be avoided and boracic fomentations kaolin poultices and glycerin and magnesium sulphate dressings often do more harm than good Dry heat may be applied with precautions to prevent burning or hot bathing may be used In the intervals between such procedures the following paint may be applied to and around the boil to control the local infection and to keep the surface of the skin dry and hard

Mercuric chloride	0 1 per cent
Brilliant green	1 0 per cent
75 per cent industrial spirit to	100 0 per cent

Once the boil is discharging dry dressings frequently changed are used and chlortetracycline cream 1 per cent or the above mentioned paint, applied to the skin around

Surgery in particular crucial incisions is contraindicated and the only justifiable

manipulative procedure is the encouragement of separation of the slough as soon as possible

Boils on the nose and upper lip need especial care because of the risk of infection spreading by communicating veins to the interior of the skull with fatal results On no account should they be subjected to pressure The patient should be rested and systemic antibiotic treatment started at once Locally the gentle application of warmth is justifiable

HYDRADENITIS SUPPURATIVA

This is an infection of apocrine glands in the axillæ or perineum often giving rise to deep abscesses which tend to track beneath the skin

Ætiology—The condition is more common in women than in men The apocrine glands are susceptible to psychosexual and endocrine stimuli Infection is unlikely to arise without some other factor being present such as chemical irritation from depilatories deodorants or the rubber of dress protectors

Clinical Picture—In one or both axillæ or at the perineum is an irregularly nodular surface with tenderness and areas of induration and of fluctuation Pus may be discharged from sinuses and there is a marked tendency to tracking irregular scarring chronicity and recurrence

Treatment—Any chemical irritation of the region should be avoided Culture and use of the appropriate antibiotic in a cream is usually effective or 0 1 per cent. mercuric chloride and 1 per cent brilliant green in 75 per cent industrial spirit may be applied In resistant cases X rays 100 r up to four times at weekly intervals may help In the most chronic forms success has followed excision of the affected tissue with plastic repair

DERMATITIS VEGETANS

This is a condition of irregular epidermal hyperplasia overlying an area of infected dermatitis where the tissue reactions are vitiated by senility or local disease in particular lymph stasis

Clinical Picture—Over an extensive area of skin there is redness with a pustular exudate and an irregular warty or even pseudo epitheliomatous hyperplasia of the epidermis Culture may reveal a mixed infection in which Gram negative organisms such as *Ps pyocyanea* and *Proteus* are prominent

The condition may develop as a complication of pre existing skin conditions for example pemphigus vulgaris

Treatment is that of the underlying condition and elimination of the causal organisms In the form secondary to lymphatic blockage in the leg the best that can be expected is an elephantiatic leg and sometimes amputation may have to be considered as likely to give the best results whereas retaining the limb may bring with it much toxicity and secondary anæmia

PYODERMA GANGRENOSUM

This is a rare condition of burrowing colliquative necrosis and ulceration of the skin either due to symbiosis between anaerobic streptococci and hæmolytic streptococci (Meleney s ulcers) or due to the loss of fluid and electrolytes that occurs in acute exacerbations of ulcerative colitis or dysentery or when massive intestinal hæmorrhages occur in the former disease A similar condition has rarely been reported in extensive cachectic states with varicella There is leucopenia due to marrow depression

Treatment is of the primary condition Replacement of fluid and electrolytes blood transfusions and antibiotics are necessary With control of the loss of fluid and electrolytes healing usually begins spontaneously

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TINEA CAPITIS (TINEA TONSURANS)

MICROSPOROSIS

Ringworm of the scalp in over 90 per cent of cases is due to microsporon either *Microsporon audouini* (the human form) or *M canis vel felineum* A much rarer form acquired from animals is *M gypseum* All forms only infect children the skin at puberty acquiring fungistatic properties

Ætiology and Pathology —The human form is believed to be spread by direct contact and by indirect contacts for example hair clippers and caps it may also be air borne The animal form is acquired by fondling kittens and puppies and may spread from child to child for two or three transferences before it loses its vitality which is re established after infection of an animal host once more

The organisms invade the stratum corneum and the mycelium grows down the hair follicles and thence passes to the hair shafts forming a mosaic of spores around the shafts and mycelial threads within the shafts The hair shafts become fibrillated and break off about 3 mm above the surface of the skin

Clinical Picture —As a general rule *M audouini* causes less severe reactions than *M canis* and is less likely to be associated with tinea of the glabrous skin The *history of animal contacts in the latter and of a school or institutional epidemic in* the former may also help to suggest the nature of the fungus

Characteristically there are circular areas of short bent or broken hairs with frayed ends and having thicker shafts than those of the unaffected scalp around The scalp itself shows a dirty scaling without redness or there may be slight papulo pustulation Rarely there are numerous follicular pustules with much œdema causing a boggy dusky dome shaped swelling a condition known as kerion This is more common with Trichophyton infections

Sometimes the circular or annular arrangement is inconspicuous or absent and casual inspection may suggest a diagnosis of infective dermatitis if the whole or most of the scalp is affected until closer inspection shows broken hairs which are not found in infective dermatitis

Examination with Wood s light is an invaluable aid to the diagnosis and management of these disorders It consists of ultra violet rays passed through a nickel glass filter With microsporon but not with trichophyton there is a brilliant green fluorescence of the affected hairs As the infection persists the fluorescence tends to become less brilliant With Wood s light the diagnosis can be made of microsporon ringworm affected hairs can more easily be removed for microscopy and culture and the follow up of patients until cure is greatly facilitated It is often noted under the lamp that single outlying hairs are affected and even that small patches are present which were not suspected on examination by daylight Direct microscopy is not essential if examination under Wood s light is positive It is carried out by extracting a hair and placing it on a slide with potassium hydroxide Heat is applied to hasten the keratolytic action of the potassium hydroxide Microscopy then reveals a mosaic of small spores surrounding the hair shaft

Diagnosis has now reached the stage of microsporosis Further differentiation is made by culture using Sabouraud s medium Usually the macroscopic and microscopic features of the culture are characteristic but occasionally dysgonic forms are seen

Course and Prognosis —The *natural history differs in the two types of infection M audouini* tends to persist indefinitely or until puberty whereas *M canis* usually dies out after about 3 months It follows that local applications may be sufficient in the latter but not in the former

Diagnosis —Alopecia areata causes smooth bald patches with exclamation mark hairs at the periphery Trichotillomania causes areas of broken off hairs usually at one temporo frontal region Infective dermatitis causes redness and scaling and

ERYSIPELAS (see p 34)

ERYSIPELOID

An infection of the cellular tissues of the fingers or hands with the organisms of swine erysipelas, from injury to the skin arising from the handling of animal or vegetable matter

Clinical Picture—This is essentially a disease of food handlers and manipulators It starts as an erysipelas like swelling on a finger or the hand The swelling advances with an easily visible border and may travel up one finger on to the hand and down the adjoining finger Constitutional disturbance is slight If untreated the condition persists for several weeks

Treatment—It quickly responds to intramuscular injections of penicillin

ANTHRAX

This is dealt with elsewhere (see p 79)

CUTANEOUS DIPHTHERIA

This is rare Wounds (for example desert sores) may be infected and occasionally lesions develop on the skin of children suffering from naso pharyngeal diphtheria The skin may also be affected without mucosal involvement

Clinical Picture—There may be only one lesion or several At first there is a blister which ruptures, a red zone develops around and a central slough forms Diphtheria may cause paronychia Constitutional symptoms are often slight but *the complications serious*

Diagnosis is from infected eczema, impetigo and ecthyma Direct smear and cultural examination for *Corynebacterium diphtheriæ* confirms the suspicion

Treatment—Diphtheria antitoxin should be given in full dosage immediately the condition is suspected *without waiting for a bacteriological report* The patient should be kept at rest and isolation is necessary Locally the area should be cleaned with cetrimide 1 per cent and an antibiotic such as chloramphenicol cream applied

FUNGOUS INFECTIONS

Mycotic infections of the skin may be superficial (epidermal) or deep (dermal) The former type is common, the latter rare

SUPERFICIAL FUNGOUS INFECTIONS

Pathogenic fungi are classified according to their morphological and cultural characteristics macroscopically and microscopically into *Microsporon*, *Trichophyton*, *Epidermophyton* For the clinician it is more convenient to classify fungous diseases according to the region of the body they are affecting The chief groups are *tinea capitis tinea barbæ tinea glabrosa tinea axillæ et cruris tinea pedis* and *tinea unguium* Two or more regions on one patient can be affected by a fungus concurrently, the zonal terminology being arbitrary For example *Trichophyton rubrum* may affect the nails the hands the feet and the groins at one time

Fungous eruptions particularly if infected with cocci or if over treated often give rise to secondary eruptions or mycides which depending on the nature of the fungus are described as microsporides trichophytides epidermophytides, favides or moniliides (levurides)

Favus may also affect the glabrous skin with scutuliform lesions in which bright yellow cups form massive crusts and it may cause nail deformity Favus is usually acquired in childhood but it persists into adult life if untreated

Treatment of scalp trichophyta depends on their natures With the animal ectothrix kerionic forms manual epilation followed by the application of Whitfield s ointment or magenta paint usually suffices It is wise to give warning of the probability of some degree of scarring The boggy swelling of kerion should not be incised

In the endothrix forms X ray epilation is usually necessary With favus it is important to examine all child contacts under Wood s light to find if any clinically undetectable early cases exist

TINEA BARBÆ

Ringworm of the beard is nearly always caused by *T mentagrophytes* or *T discoides* infections of animal source hence it is found mostly amongst grooms and farm workers It presents as irregular areas of follicular papulo pustulation in the beard area, with considerable perifollicular swelling which gives rise to the fig like nodular appearance of mycotic sycosis Microscopy of an extracted hair often fails to reveal the fungus because of a secondary coccal infection as in kerion celsi

Treatment is by manual epilation and the use of fungistatics for example Whitfield s ointment or Castellani s paint X ray exposures of 150 r up to four times at weekly intervals may be used to diminish the swelling and tendency to keloid formation

TINEA GLABROSA

Tinea of the glabrous skin may be classified for clinical purposes as tinea circinata of body and limbs tinea axillæ et cruris and tinea pedis

TINEA CIRCINATA

This form of ringworm affects children or adults and may be due to microsporon or trichophyton The former may occur in children with tinea capitis due to *M canis* or in adults coming into contact with them The latter may be of human or animal source In nearly all forms the infection spreads peripherally and heals centrally with the result that the early macular or papulo vesicular lesion becomes a ring with a scaly or vesicular border and a central zone of normal or discoloured skin In infections by *T discoides* (cattle ringworm) groups of papulo pustules occur on the forearms or on the backs of the hands but the endothrix trichophytons tend to form large rings

Diagnosis is from pityriasis rosea patchy infective (seborrhoeic) dermatitis nummular eczema

Pityriasis rosea begins with a herald patch followed by a general eruption but microscopy reveals no fungus

Discoid infective dermatitis has greasy scales a sweat area distribution and signs of infective dermatitis elsewhere

Nummular eczema presents with papulo vesicular disks on the forearms and hands calves and feet

Treatment.—Tinea circinata is usually eliminated easily with fungistatic agents such as Whitfield s ointment, magenta paint or weak tincture of iodine If the patient is a child it is important to examine the scalp under Wood s light even in the absence of clinical evidence of involvement of the scalp

In the pustular form it is advisable to carry out manual removal of any hairs present.

loss of hair but no *breaking of the hairs Impetigo of the scalp is* more exuberant and lesions are usually present elsewhere, or there is some other cause for it such as pediculosis

Treatment —Scalp ringworm is a problem in epidemiology With *M audouini* it is necessary to examine the contacts and to trace the infection to its source if possible A Wood s light is invaluable for this purpose In residential institutions tracing the source and quelling the infection is relatively simple In day schools it may be difficult because *siblings of all the school contacts should be examined as well* Fortunately as microsporosis is almost unknown after puberty, it is not necessary to examine children over 14 years of age

Treatment should be begun with local applications pending the cultural diagnosis The choice of local application is, at present relatively unimportant as one is not available which will eliminate the infection from the depths of follicles and from the hair shafts themselves which is the essential of cure Local applications serve the purpose of fungistatic action on the surface and at the ostia and prevent contaminated fragments of scale or hair from being carried off in the air

The mother is instructed to cut the hair all over the head to stubble and to make two linen closely fitting skull caps for continual wear, on alternate days, the cap not in use being boiled The scalp is scrubbed daily with soap and water paying special attention to the areas known to be affected Then the ointment being used (Whitfield s ointment or phenyl mercuric nitrate 0 5 per cent in emulsifying ointment or dithranol 0 5 per cent in emulsifying ointment) is scrubbed into the scalp with enough vigour to cause a slight erythematous reaction

In small spore ringworm of the scalp due to *M audouini* it is exceptional to get a cure with local applications and recourse is had to X ray epilation using either a *4 or a 5 circular fields method The hair falls after 3 weeks when examination* under Wood s light will reveal any affected hairs that may remain These can be removed gently with epilation forceps In the epilating stage a fungistatic ointment, for example Whitfield s should be applied and the falling hair burned Epilation by *thallium acetate (8 mg per kg of body weight) in a single dose is too dangerous* a method and has been practically abandoned death having occurred from accidental overdosage

RARER FORMS OF SCALP RINGWORM

Large spore ringworms of various types may affect the scalp They include two *forms contracted from animals T mentagrophytes from domestic or* farm animals and *T discoides* from cattle Both are ectothrix forms In the former filaments and spores are seen around the hairs in the latter large spores Four endothrix forms all of human origin include *T tonsurans*, *T sulphureum T violaceum* and *T schoenleini* (favus) None of these forms of scalp ringworm causes fluorescence under Wood s light, except favus which gives a pale bluish green fluorescence throughout the length of the hairs which often remain unbroken

Microscopically the endothrix ringworms show filaments and spores within the hair shafts Favus may be recognisable at this stage by its polymorphic filaments and oval spores with areas having the appearance of air spaces within the shafts

Clinically the trichophyta of animal origin usually cause kerion but the endothrix *forms cause much less violent reactions* perhaps some scattered broken hairs with thick scurf with *T violaceum* the hairs break off flush with the surface of the skin (black dot ringworm) giving an appearance that can easily be confused with alopecia areata Microscopy after careful removal of a hair reveals the fungus as mycelial threads and oval segments Favus may resemble infective dermatitis mousey smelling, yellow scutuliform scales may be present or in long standing cases where the scalp has been kept clean it may present as a slowly extending cicatricial alopecia

changed daily or a fresh pair of white cotton in socks can be worn each day Sponge rubber soles should not be worn The feet should be washed twice a day and magenta paint applied at night and 3 per cent salicylic acid powder liberally shaken into the socks and between the toes each morning Mercurial fungicides are liable to sensitise the skin and zinc undecylenate is relatively ineffective Whitfield s ointment is some times useful or 1 per cent silver nitrate lotion If any secondary infection is present foot soaks in potassium permanganate 1 in 6000 for 10 minutes twice a day are useful

TINEA UNGUIUM

Ringworm of the nails may be due to trichophyton or epidermophyton It may pick out one nail one hand or foot or both It is unusual for all the nails to be affected and the distribution is usually asymmetrical

Clinical Picture —The nails are usually affected from their free edges and become grey or brown thickened rough dull friable and honeycomb like They are sometimes easily shed To make a microscopic examination for fungus a micro scope slide is used by scraping with its edge fine flakes of nail can be detached The more superficial ones are discarded the deeper ones are caught on another slide covered with potassium hydroxide and a cover slip and heated to hasten the keratolytic action of the potassium hydroxide It is usually easy to find mycelium by this method but subsequent attempts at culture often fail

Diagnosis —Ringworm of the nails has to be differentiated from psoriasis eczema syphilis and nail dystrophies Psoriasis usually affects many nails in sym metrical fashion Thimble like pitting may be present or the nails may be thickened and yellow In tinea unguium there may be only one or two nails affected and the discoloration is dirty grey rather than yellow Microscopic examination for mycelial filaments is the deciding method in doubtful cases in addition to the presence or absence of psoriasis or fungous disease elsewhere Paronychia is rarely caused by pathogenic fungi but often in part due to monilial infection

Treatment —The eradication of fungous infections of the nails is very difficult and success is exceptional Removal of the nail plates and the application of fungi cides to the nail bed is usually followed by recurrence X ray exposures and thorium X applications have sometimes been reported to give partial success Useful local applications include ammoniated silver nitrate $\frac{1}{2}$ per cent dithranol ointment and zinc undecylenate ointment but the most that can be said for each and all of these is that they may help to check the spread of the disease on the sufferer and to others It is important to treat concurrently any skin areas involved

MONILIAL INFECTIONS

Monilia (candida) albicans may affect the mucosæ and skin in several ways monilial stomatitis (thrush) monilial vulvovaginitis monilial intertriginous dermatitis monilial paronychia

Monilial stomatitis occurs as thrush in infants with white easily detached shreds overlying the mucosæ In adults monilial stomatitis may follow the use of anti biotics which disturb the flora of the mouth

Angular stomatitis is sometimes infected with monilia

Monilial vulvovaginitis is a cause of pruritus vulvæ and usually presents as a shiny flexural erythema with a heaping up of white sodden epidermis at the margin

Monilial flexural dermatitis has a similar appearance at other sites chiefly under pendulous breasts or abdominal folds at the umbilicus at axillary and genitocrural flexures and between the fingers in the form known as *erosio interdigitalis mycotica* It is a common cause of sodden skin in the toe clefts

In all these forms of monilial dermatitis it is important to test the urine for sugar and to look for evidence of nutritional deficiency

TINEA AXILLARIS ET CRURIS

This presents as extensive areas of erythema in the *flexures with festooned poly cyclic* edges showing some scaliness or slight vesiculation from which mycelium can be recovered The anal region, the perineum, the scrotum and the buttocks may *be affected as well as the genito crural folds* The responsible organism is usually either *T rubrum* or *Epidermophyton floccosum* either may also affect the hands feet and nails but *E floccosum* does not affect the hair

Diagnosis —In infective dermatitis of the flexures there are numerous follicular erythematous "satellite' lesions In ringworm of the axillæ and groins (eczema marginatum) *these are not present In doubtful cases microscopy should make the* diagnosis clear In flexural dermatitis due to hæmolytic streptococci the intensity of inflammation is much greater and in monilial dermatitis the white sodden epidermis overlying the moist, reddened surface with fissuring in the depths of the folds makes the diagnosis clear Contact dermatitis due to textiles is recognised by its preference for the folds of the axillæ rather than their domes

TINEA PEDIS

This is usually due to *T mentagrophytes*, *T rubrum* or *F floccosum* Cultural differentiation is important because eradication of *T rubrum* is a far more difficult *matter than eradication of T mentagrophytes* or *E floccosum*

Ætiology —Foot ringworm is most easily spread where people mix in bare feet hence its designation 'Athlete s Foot Sports clubs swimming baths and bath rooms are probably the commonest sources of contagion but individual susceptibility because of hyperidrosis crowded toes and minor foot deformities is also important *Other factors include climatic and working conditions of heat and humidity* and faulty footwear, in particular thick socks and impervious footwear

Clinical Picture —On the inner surface of the foot spreading on to the sole, groups of vesicles are present of various sizes and of skin colour Secondary *infec* tion may cause opalescence of the vesicles The eruption is usually somewhat asym- metrical Other parts of the sole may be infected especially the flexures and clefts of the toes but when the only physical sign is white sodden skin with fissuring of the fourth toe clefts monilial intertriginous dermatitis is a more likely diagnosis

In the presence of secondary infection or over treatment a secondary eruption (mycide) of vesicles often develops symmetrically on the hands and feet These vesicles do not contain fungus and the hand condition is in no way contagious Infec tion may however spread to the nails of hands and feet

T rubrum infections behave in a different fashion It is not unusual to find simultaneous infection of the hands feet nails and groins The hands and feet usually show a diffuse fine peeling and some redness only perhaps with hyperkera tosis and fissuring but without vesiculation often the condition is unilateral One *or more nails may be affected as well* On the calves there may be discrete deep follicular lesions resembling a deep coccal folliculitis tuberculide or even erythema nodosum

Diagnosis —Microscopic confirmation by *removing the roofs of suspected* vesicles is essential if errors are to be avoided as a very similar if not identical picture can arise in pompholyx (dysidrosis) and in contact dermatitis Contact eczematous dermatitis of the feet usually arises on the dorsa but may itself be due to over treat ment of tinea pedis Tinea pedis is often asymmetrical whereas pompholyx is sym metrical Sodden toe clefts may be due to excessive sweating and maceration or to monilial infection

Pustular psoriasis of the feet presents as reddened areas with excessive scaling and brown pustules ' *which are sterile on culture* and microscopically show no fungus

Treatment —Footwear should be well fitting socks should be of cotton and

Treatment consists of shaving followed by the application of calamine lotion with 2 per cent of sulphur

MYCIDES

These may take the form of vesiculation of the hands (pompholyx) or lichenoid horny follicular papules in groups on the trunk (lichen trichophytide) Erythematous urticarial erythema multiforme and erythema nodosum types have been described

Treatment is by bland local applications while the primary focus is being got under control

DEEP FUNGOUS INFECTIONS

These conditions are rare in Great Britain

SPOROTRICHOSIS

This is caused by accidental inoculation with *Sporotrichum schencki* a plant sapro phyte Infection usually takes place through the hand or forearm and vegetable handlers or persons attending to animals are most likely to be affected There is a primary lesion at the portal of entry an ascending lymphangitis and chains of nodules which break down and suppurate along the course of the lymphatics

Clinical Picture —There may be cutaneous mucosal or systemic manifestations There may be a chancre like lesion with lymphangitis and lymphaden tis and multiple subcutaneous cold abscesses which break down to form gummatous or ecthymatous ulcers with little or no pain Apart from the skin cold abscesses may form in the mucosæ muscles lymph nodes joints bones epididymis lungs gastro intestinal tract or the central nervous system

Diagnosis is from late syphilis halogen eruptions other fungous infections and the primary tuberculous complex The lymphatic spread is typical of sporotrichosis Syphilitic gummata are usually single or few in number The primary tuberculous complex has a portal of entry and an ulcerated lymph node draining it but not chains of ulcers along the lymphatics as in sporotrichosis Halogen eruptions may be granulomatous and ulcerative but are usually symmetrical and do not have a distribu tion corresponding to a lymph drainage area In sporotrichosis there are multiple lesions in lymphatic distribution with little constitutional disturbance

Treatment —Potassium iodide in ascending dosage up to the limits of toleration usually brings about a steady resolution

BLASTOMYCOSIS (GILCHRIST S DISEASE)

In the localised form of this infection with *Blastomyces dermatidis* papulo-pustulation goes on to the formation of large ulcers bordered by papillomatous vege tations and with discharging sinuses and epidermal bridges The proliferation of the epidermis may be so marked as to resemble epithelioma (pseudo epitheliomatous hyperplasia) In the systemic form the lungs are most commonly affected but no organ is immune

Course and Prognosis —The condition is benign but chronic

Diagnosis is from syphilis sporotrichosis halogen granulomata vegetating pyo derma tuberculosis verrucosa cutis and epithelioma Repeated microscopic and cultural search may be necessary before the budding yeast fungus is demonstrated The histology resembles tuberculosis but with blastomyces in the centre of a nodule

Treatment is by thorough curettage and cautery of the extending hyperplastic edge X ray therapy is usually ineffective Potassium iodide in large doses should be given a trial

Monilial paronychia—The cause of chronic paronychia is a break in the epidermal barrier due to the effects of alkalis, detergents cuticle removers or excessive manicuring Once this barrier is broken down *Staphylococcus saprophyticus* and yeasts gain access to the folds and cause a low grade inflammation If the hands are repeatedly immersed in alkaline solutions or if they are exposed to beer as with barmaids cleaning up bar counters conditions are rendered ideal for the infection to develop

Treatment of monilial infections consists of attention to the general health, attention to the local anatomical condition predisposing to this infection and the application of fungicides

Unbalanced nutrition obesity and any associated diabetes must be controlled Opposing skin folds should be prevented from rubbing against one another by means of suitable dressings up lift brassieres and abdominal supports well fitting socks and shoes The affected areas should be kept clean with an unscented toilet soap and after its use a talcum dusting powder should be liberally applied to the less active areas and magenta paint to the more active ones To any fissures in the depths of the folds a 2 per cent solution of silver nitrate applied daily by an orange stick is usually effective

Monilial paronychia can only be relieved with full co operation on the patient s part Wet work must be kept to a minimum and the handling of soda, alkaline soaps and detergents is forbidden Magenta paint is allowed to trickle under the nail folds by means of a camel hair brush X ray exposures to the folds (150 r) weekly or fortnightly on up to four occasions are often invaluable in encouraging the re growth of the epidermis over the proximal parts of the nail plates After cure the patient must be reminded of the possibility of recurrence and advised to take especial care to avoid the known hazards

TINEA VERSICOLOR

Malassezia (microsporon) furfur is the organism responsible for this condition which presents as brown, slightly scaly plaques on the body and to a lesser degree on the limbs If the skin has been exposed to sunlight the affected areas may be paler than the normal areas adjoining (achromia parasitica) The affected areas are also pale in coloured people

Diagnosis—In tinea versicolor in the white man the brown areas are ' islands in a ' sea of white and the edges of the brown are convex In vitiligo the converse applies In tinea versicolor there is slight scaling made more apparent by scraping the edge of brown Microscopic examination of these scales reveals fragments of mycelium and many spores sometimes in clusters resembling bunches of grapes This fungus will not grow on artificial media Another diagnostic feature is a golden fluorescence when the patient is examined under Wood s light

Treatment—Tinea versicolor is encouraged by hyperidrosis or sweat retention hence it is wise to look for any tuberculous or other condition which might be responsible for the sweating Insufficient bathing and the wearing of the same thick woollen underclothing day and night may be to blame Bad habits of this sort must be corrected and porous underclothing worn and changed daily if the condition is to be cured The application of 10 per cent sodium thiosulphate is effective or the 3 per cent ointment of sulphur and salicylic acid may be applied Treatment should be continued for 2 weeks after apparent cure The bed linen and underclothes should be disinfected by laundering

LEPOTHRIX (TRICHO MYCOSIS AXILLARIS)

This is a fungous infection around hairs in the axillæ producing dark reddish concretions and caused by *Nocardia tenuis* in symbiosis with a coccus which forms red yellow or black pigment

Inoculation through the skin may happen when contaminated dust is accidentally abraded into the skin as when an infant crawls on the floor in a house in which there is a patient with open pulmonary tuberculosis Lupus most commonly begins in the first decade but occasionally starts much later in life The face particularly around the orifices is the commonest site of infection but the elbows hands knees buttocks and perianal region are other relatively common sites Local spread then proceeds by the lymphatic channels or these vessels may be the route by which an infection primarily infecting the nose reaches the skin Involvement of the skin by spread from underlying tuberculous foci takes place in scrofuloderma (King s Evil) from the breaking down of cervical tuberculous lymph nodes also from sinuses draining tuberculous kidneys bones and joints Spread by the blood stream only occurs in states of extreme debility which may arise with measles or pertussis In this form multiple foci may occur on widely separated parts of the skin In its extreme form of severity blood dissemination causes the rare and often fatal condition of tuberculosis cutis miliaris acuta or lupus miliaris in which the multiple miliary areas of tuberculosis are only the outward signs of a miliary tuberculosis of internal organs

Typical tubercles are seen in the dermis with round cells surrounding a zone of epithelioid and giant cell histiocytes There is considerable disruption of collagen with a variable amount of fibrous tissue formation Secondary epidermal changes may include atrophy and a patchy parakeratosis but at some sites for example the hands and buttocks warty thickening may occur (lupus verrucosus)

Clinical Picture —The nodule of lupus vulgaris is a flat semitranslucent area with slight scaling—the apple jelly' nodule described by Jonathan Hutchinson Subsequently the lesion may have exudative or fibrotic characters In the former there is some swelling and redness and no tendency to heal spontaneously ulceration may occur In the fibrotic form the lesions are not raised and ulceration does not occur but the lesions tend to heal in places with much scarring only to break out once more here or elsewhere As a result multiple foci of activity may remain amongst extensive areas of scarring

Lupus around the nose and mouth is often complicated by mucosal lupus in the nose or on the gums cheek tongue palate pharynx or larynx Mucosal lesions are different from the cutaneous ones being dusky granular infiltrations which bleed easily

Lupus vulgaris may destroy cartilage but not bone The resultant deformities that may arise include simian or parrot bill deformities of the nose due to destruction of the alæ and septum respectively septal perforation and stenosis or occlusion of the anterior nares The mouth may be narrowed by scarring (microstomia) or the upper lip may be retracted permanently exposing the gums Contracture of scarring below the eye often causes ectropion The pinnæ may be destroyed irregularly or completely or they may as a result of the inflammatory process become adherent to the skull Some of these deformities are in part due to secondary infection or to the use of caustics and X rays in treatment Lesions on the limbs and body may be very extensive Ulceration may be followed by scarring and contractures or lymphatic obstruction may lead to elephantiasis

Complications of lupus include secondary infection particularly in the nose contractures elephantiasis and the development of keratoses and prickle cell carcinoma This is particularly likely to happen in patients who have received X ray treatment for the lupus but it may also occur in patients who have had much treatment by ultra violet irradiation and other locally destructive procedures

Lupus vulgaris may be associated with phlyctenular keratitis tuberculosis of the upper respiratory tract of bones joints or kidneys and rarely of the lungs

Diagnosis —The earliest lesions may resemble moles but on diascopy (inspec tion through a piece of glass firmly applied to the skin) it is clear that the brown colour is due to an exudative process and of apple jelly appearance whereas with moles and

ACTINOMYCOSIS

This condition is due to bacteria like fungi of genera Nocardia Actinomyces or Streptothrix The cutaneous form (cervico facial) causes dermal infiltration leading to indurated irregular subcutaneous nodulation going on to ulceration, with sinuses from which seropurulent or sanguineous fluid containing sulphur yellow granules is discharged Further nodules form nearby with boardlike hardness The skin may also be involved secondarily from deeper involvement in the mouth thorax or abdomen The tongue lungs, intestines, urinary tract female genitalia or bones may be affected

Histology—A granule consists of one or more colonies each of which has mycel lium and pigment granules in the central zone and club shaped organisms in palisade arrangement at the periphery The branching hyphæ are Gram positive

Course and Prognosis—The course is slow, the malady sometimes persisting for up to 10 years

Diagnosis from syphilis sporotrichosis scrofuloderma and carcinoma is made from a consideration of the clinical bacteriological and histological findings (*q v*)

Treatment is by penicillin or other antibiotic Surgery and X irradiation may also be of value

CUTANEOUS TUBERCULOSIS

The skin may be invaded by tubercle bacilli or it may be the site of reactions of hypersensitivity to these organisms (tuberculides) When the skin is invaded by tubercle bacilli its manner of response depends on the immunological state of the host at the time If the individual has suffered no previous tuberculous infection at any site the Mantoux reaction is negative (primary anergy) and the response will be the primary tuberculous complex but if there has been a previous tuberculous infection in the skin or elsewhere, and the Mantoux reaction is positive the response will be lupus vulgaris (normergy) It is believed that if a secondary anergy develops any subsequent tuberculous infection causes the condition known as sarcoidosis, although this reaction may also be non tuberculous Some individuals develop an excessive sensitivity to tuberculin In them tuberculous infection at any site may be followed by some form of tuberculide (hyperergy)

THE PRIMARY TUBERCULOUS COMPLEX IN THE SKIN

This consists of a tuberculous chancre on some exposed part of the body such as the face eye hands or knees and enlargement of the lymph node draining the area The chancre resembles a boil but instead of suppurating it persists as a crusted indurated patch with a little bloodstained discharge The lymph node draining the site enlarges softens and breaks down through the skin leaving an irregular scar Subsequently the primary chancre slowly heals up or it may form the focus from which a patch of lupus vulgaris develops The Mantoux reaction changes from nega tive to positive with the development of the primary complex

Diagnosis has to be made from a low grade coccal infection

LUPUS VULGARIS

Ætiology and Pathology—Infection of the skin causing lupus vulgaris may take place by inoculation by lymphatic spread by the breaking down of some under lying tuberculous focus or by the blood stream Either human or bovine bacilli may be responsible

effect as well as helping by the formation of vitamin D in the skin Light treatment still has its uses to day when dealing with solitary resistant foci for which a course of isoniazid may be considered unjustifiable

LUPUS VERRUCOSUS (TUBERCULOSIS VERRUCOSA CUTIS)

This is usually due to inoculation from without It most commonly occurs on the hands or buttocks as a violaceous warty excrescence with a reddish halo and a sero purulent discharge One form of it is the verruca necrogenica the anatomical tubercle or post mortem wart acquired from a human or bovine cadaver but the infection can also occur from a patient s own tuberculous sputum The lesions may be secondarily infected but they do not ulcerate Dissemination of tubercle bacilli may occur from them through the lymphatics to lymph nodes and the blood stream The histological appearance is of a nonspecific inflammatory reaction with overlying papillomatosis or there may be a tuberculoid appearance

Diagnosis is from warts lichen planus verrucosus syphilis vegetating pyoderma and blastomycosis Warts do not show dusky discoloration Lichen planus verru cosus usually occurs on the shins or on the forearms and itches intensely Syphilis is much more actively inflammatory than the indolent lupus verrucosus Vegetating pyoderma and blastomycosis can only be differentiated by histological and cultural methods

Treatment is by surgical excision curettage and cautery or by oral treatment with isoniazid

TUBERCULOSIS COLLIQUATIVA (SCROFULODERMA)

This is tuberculosis of the skin secondary to tuberculosis of underlying lymph nodes joints or bones

Clinical Picture —The commonest form is in the neck secondary to tuberculous cervical adenitis Subcutaneous nodules become attached to the skin which becomes dusky and indurated finally the mass breaks down and a crusted sinus is exposed or ragged undermined ulcers form with intercommunicating sinuses When the condition heals irregular scarring is left

Diagnosis from syphilis actinomycosis and sporotrichosis is on clinical grounds and by cultural serological and histological methods

Treatment is by attention to good feeding housing and fresh air general ultra violet irradiation and isoniazid by mouth 300 to 400 mg daily Surgical intervention is sometimes necessary

TUBERCULOSIS CUTIS ORIFICIALIS

This is a form of painful tuberculous ulceration in or around the orifices usually secondary to tuberculosis of internal organs thus tuberculous ulcers of the nose palate tongue floor of mouth or the lips arise from infection by sputum from a pul monary or laryngeal focus ulceration of the external genitalia in both sexes may occur from tuberculosis of the genital or urinary tracts Perianal ulcers may occur in persons with intestinal tuberculosis The ulcers are painful shallow and ragged with undermined edges and dirty grey bases from which there is a mucopurulent secretion

Diagnosis is from chancre epithelioma or chancroid by bacteriological examina tion from the base of the ulcer

Treatment is by electro cautery or chemical cautery with acid nitrate of mercury and with isoniazid by mouth

TUBERCULIDES

These are skin reactions which are due to hypersensitivity (hyperergy) to tuber culin In some forms this relationship is clearly established in others it is suspected but not proven

freckles it is duller and without translucency More advanced lesions have to be differentiated from syphilis, tuberculoid leprosy sarcoidosis, lupus erythematosus lupoid sycosis and rodent ulcers Lupus vulgaris usually starts in the first decade affects skin and cartilage and takes years to develop, showing characteristic apple jelly nodules Syphilitic gummata develop much more rapidly, usually in the 30 to 50 age group and may ulcerate and destroy in weeks or months to an extent that would take lupus several years Bone may be destroyed as well as cartilage and skin and it is not unusual for a gumma to form deeply and to ulcerate rapidly with the formation of a large cavity perhaps involving the maxilla Tuberculoid leprosy may closely *mimic lupus but there is anæsthesia* to light touch, and heat and cold, the nerves in the area may be thickened and tender and the patient has lived in an area of endemic leprosy

Sarcoidosis presents as raised, pinkish yellow, translucent nodules about the face or on the shoulders and arms, or as indurated erythematous lesions on the legs Histological study may be necessary in the differentiation

Lupus erythematosus is often symmetrical and involves the "bat's wing' area of the face, the scalp (which is seldom affected by lupus vulgaris) the vermilion surface of the lips and perhaps the backs of the fingers There is redness with follicular plugging, scaling and central atrophic scarring but without apple jelly nodulation A very important differential point from lupus vulgaris is that lupus erythematosus never involves cartilage so that no matter how long it has been present there is no serious deformity of nose or ears and no loss of tissue other than the skin

Rodent ulcer may be simulated by ulcerated lupus but it has a hard pearly edge, whereas ulcerated lupus is ragged Lupus vulgaris may be complicated by squamous cell epithelioma

Ancillary aids to differential diagnosis include biopsy, the Wassermann reaction the *Mantoux reaction the Kveim test and the lepromin test*

Treatment of lupus has been revolutionised in the last few years Isoniazid in a dose of 300 to 400 mg a day leads to disappearance of the nodules and of scaling within 2 to 6 months almost without exception Time alone can tell of the permanency of this effect because with all treatments of lupus vulgaris 'cure can only be considered a possibility after 5 years uninterrupted clinical clearance In the present state of knowledge a course of 6 to 12 months seems necessary There is no evidence of the development of drug resistant organisms Toxic reactions are slight and rare Histologically the nodules gradually become nonspecific and finally disappear Under an *umbrella* of isoniazid it is *possible to day for the surgeon* to carry out plastic repairs with far greater confidence than in the past

Calciferol either by local injection (300 000 units once a fortnight) or orally (150 000 units daily) is also effective but in a different way The lesions at first become worse, redder and more swollen then become less conspicuous with much fibrosis Histologically the tubercles remain but they are surrounded by an increased fibroblastic and fibrotic reaction Toxicity is a far greater hazard with calciferol The urine should be tested fortnightly and blood urea estimations carried out If the blood urea rises above 70 mg per 100 ml it is advisable to suspend the treatment Early symptoms of intoxication are euphoria capricious appetite *vomiting diarrhœa* or constipation headaches and vertigo

The general health domestic and occupational surroundings and nutrition of the lupus patient should always receive attention The diet should include ample milk butter and eggs Coexistent tuberculosis in other organs is not uncommon particularly in lymph nodes bones joints and kidneys rarely in the lungs

Before the introduction of calciferol and isoniazid the local treatment of lupus vulgaris mainly consisted of destructive measures with the Finsen Lomholt lamp, the Kromayer lamp and by chemical caustics such as the acid nitrate of mercury General ultra violet irradiation is also valuable *It has an unexplained* tonic

ACNE SCROFULOSORUM

This also affects children and adolescents who have some form of tuberculosis elsewhere The lesions especially appear on the buttocks and thighs they are red acuminate follicular papules and pustules The Mantoux reaction is positive

Diagnosis from staphylococcal folliculitis is by the more prolonged course of the tuberculous lesions and their lack of response to antibiotics

Treatment is of the primary condition and general measures to raise the resistance

PAPULONECROTIC TUBERCULIDES

Papulonecrotic tuberculides have various forms and distributions some are truly tuberculous but others may in fact be virides Superficial forms have been called follicles deeper ones acnitis Papulonecrotic tuberculides of the extremities consist of discrete inflamed papules which undergo central necrosis ulcerate form scabs and heal with scarring They occur on the extensor aspects of the forearms and legs and on the backs of the hands and feet The whole process may take some 8 weeks but there may be successive crops The Mantoux reaction may be normergic or hypoergic.

Lupus miliaris disseminatus faciei consists of multiple pinhead sized flat, discrete semitranslucent lesions which occur symmetrically on the posterior halves of the cheeks They are probably tuberculous the Mantoux reaction being strongly positive

ACNE AGMINATA

This is a condition in which acneiform apple jelly like nodules occur on the nose eyelids and face often grouped together They may also occur on the genitalia After a variable persistence they may disappear with slight pock like scarring The Mantoux reaction is usually hypo or anergic and the condition is not proven to be tuberculous it may be of virus origin (see Acneiform Eruptions)

ROSACEOUS TUBERCULIDE OF LEWANDOWSKY

This condition of translucent pink papules on the forehead cheeks and chin resembles rosacea The Mantoux reaction is strongly positive It may be a tuberculide localised by a rosaceous circulation

Histopathology of the Tuberculides—All these lesions show a tuberculoid structure but this does not of necessity prove a tuberculous ætiology A tuberculoid structure is often seen in acne vulgaris and in rosacea

SARCOIDOSIS (BENIGN LYMPHOGRANULOMATOSIS)

This is an infiltrative and nodular disease affecting the skin and internal organs

Ætiology and Pathology—Controversy persists as to the cause of sarcoidosis It appears to be an unusual type of reaction to the tubercle bacillus but it may also occur in relationship to leprosy syphilis foreign bodies or beryllium The Mantoux reaction is negative an acquired anergy to tuberculin it is probable that this anergy is sometimes more general

Histologically there are naked tubercles well defined concentric aggregates of epithelioid cells without any necrosis or marked surrounding inflammatory reaction There may be a few giant cells Tubercle bacilli cannot be found In older nodules fibrosis predominates

Clinical Picture—Most patients are middle aged adults women more often than men There is often very little disturbance of general health but there may be slight pyrexia Sarcoidosis has extremely variable cutaneous manifestations There

ERYTHEMA NODOSUM

This is a nonspecific reaction of hypodermal vascular hypersensitivity one of the causes of which is a recently developed tuberculin hyperergy (see Erythema Nodosum)

ERYTHEMA INDURATUM

Erythema induratum or Bazin s disease is a condition of dusky, painful nodulation on the lower halves of the legs of young women with perniotic "billiard table legs A faulty peripheral circulation seems to predispose to this malady which is rarely, if ever seen in males or in women with an efficient peripheral circulation The indurated areas are painful and tender and may break down and form ragged ulcers with undermined edges secondary coccal infection may follow The malady is usually bilateral The Mantoux reaction may be hyperergic normergic or hypo ergic

Pathology—There is a heavy infiltrate in the hypoderm replacing the fat The infiltrate also involves the deeper parts of the dermis It may be specifically tuber culoid in some areas and nonspecific in others The vessels show marked proliferative changes and obliterative thromboses are seen Caseating necrosis may extend up wards from the hypoderm and lead to ulceration

Clinical Picture—The bluish calves show in their lower thirds on their postero medial and postero lateral aspects irregular hard dusky painful plaque like nodula tions which often necrose centrally and leave depressed scars There may be no other sign of tuberculosis or there may be a history of a pulmonary infection or of the presence of tuberculides elsewhere for example of the papulonecrotic variety

Course and Prognosis—The changes in the hypoderm are to some extent, irreversible, and some degree of scarring is inevitable

Diagnosis is from subcutaneous (Darier-Roussy) sarcoids erythema induratum of Whitfield and syphilitic gummata In sarcoidosis there are often other lesions elsewhere on the skin and ulceration is unusual In Whitfield s erythema induratum middle aged women are mostly affected and the lesions are multiple Syphilitic gummata are painless often single ham coloured serpiginous ' punched out ' ulcers

Treatment is by elastic supports good food, housing and fresh air general ultra violet irradiation (provided there is no pulmonary focus) and isoniazid 300 mg daily Calciferol is contraindicated It may cause rapid softening of the lesions and extensive ulceration or an outcrop of papulonecrotic tuberculides Ulcerated lesions may need appropriate antibiotics to control secondary infection apart from this they should be treated in the same way as hypostatic ulcers (*q v*)

LICHEN SCROFULOSORUM

This is a rare form of tuberculide consisting of lichenoid papules which usually occurs in children with tuberculous lymph nodes bones or joints

Clinical Picture—There are brownish red lichenoid follicular papules scattered or grouped in circles sometimes with a spiny tip slight scaling crusting or even pustulation The lesions mostly appear on the trunk and there is slight itching The Mantoux reaction is strongly positive

Diagnosis is from lichen planus This is rare in children and usually causes severe itching The lesions are violaceous polygonal papules with a waxy surface In doubtful cases the histology is diagnostic the papules of lichen scrofulosorum having a tuberculoid structure

Treatment is of the underlying tuberculous condition

Ætiology and Pathology —The cause is a delicately balanced host virus relation ship easily disturbed in favour of the virus Infection with herpes virus takes place in infancy and the immunological state that results usually prevents outbreaks of herpes except when there is a severe upper respiratory infection

Histologically there are intra epidermal unilocular or multilocular vesicles with swollen grossly degenerate epidermal cells

Clinical Picture —Outbreaks may occur occasionally with severe infections or frequently and from insignificant or even undetectable stimuli Precipitating causes include coryza slight pyrexia exposure to sunlight menstruation digestive upsets and emotional stimuli Genital herpes may occur after intercourse with one partner but not with another

The outbreak begins with the appearance of a group or groups of painless reddened papules rapidly becoming vesicular The lesions may be bilateral The vesicles may remain intact or rupture forming golden scabs on an erythematous base The lesions occur most commonly on the vermilion surface of the lips around the mouth or on the cheeks ears or nose they may occur on the buttocks or on the external genitalia There is no enlargement of the regional lymph nodes unless secondary infection occurs as is not unusual An associated oral aphthosis is un common

Uncomplicated lesions pass through their various stages and resolve in 10 to 14 days Recurrences may occur as often as once a fortnight or only very occasionally the lesions recurring at the original sites or nearby especially on the cheeks lips genitalia or buttocks

Course and Prognosis —The condition is not amenable to present methods of treatment and may recur indefinitely

Diagnosis is from zoster and from impetigo

Zoster is a nonrecurrent unilateral painful malady with enlargement of the regional lymph nodes The lesions conform to a posterior nerve root (or roots) distribution

Impetigo is characterised by golden stuck on crusts or by purulent blebs and usually there are other lesions on the face in the nostrils or at the paronychial folds This differential diagnosis is one of the most important and recurrent problems of dermatology the misdiagnosis of herpes simplex as impetigo often being followed by unsuitable treatment and the development of a contact eczematous dermatitis

Herpes preputialis forms shallow ulcers which do not enlarge This helps to differentiate them from syphilis and soft sore but a dark ground examination should be made in any suspicious circumstances

Treatment —There is at present no specific treatment for herpes simplex Precipitating factors should receive attention when discovered Local applications should be bland for example calamine liniment antibiotics are best avoided An individual attack can be shortened by a single X ray exposure of 100 r but this procedure should not be used except for some special occasion It has been claimed that repeated vaccination with calf lymph sometimes checks recurrences

ZOSTER (ZONA HERPES ZOSTER SHINGLES)

An eruption of vesicles in unilateral segmental distribution

Ætiology and Pathology —The cause is an infection of the posterior nerve roots and corresponding area of the skin with the virus of varicella The virus may be activated by infections neurosyphilis neoplasms Pott s disease of the spine Hodgkin s disease and other reticuloses certain drugs particularly arsenic or deep X irradiation but usually no such cause is apparent

Zoster may coincide with one or several vesicles of varicella elsewhere on the

may be raised, dome shaped nodules with an apple jelly appearance on diascopy or more deeply situated lesions causing purplish or skin coloured opaque nodules or plaques with fine vessels coursing over the surface The more superficial lesions (sarcoidosis of Boeck) appear especially on the nose cheeks lips shoulders and upper limbs The deeper lesions (Darier Roussy sarcoids) appear on the face and extensor aspects of the limbs including the sarcoid variant of erythema induratum on the legs Diffusely infiltrating erythrodermatous, annular and serpiginous forms of sarcoidosis are also described

In one form (lupus pernio of Besnier) the nose, ears hands and feet are dark blue, swollen and doughy but not cold Sarcoidosis may affect practically any organ in the body, causing mucosal lesions uveoparotitis hilar glandular enlargement or pulmonary infiltrations, enlargement of lymph nodes, tonsils, spleen liver, breasts testes, etc, disturbances of the gastro intestinal, genito urinary systems, peripheral or central nervous systems The iris and the choroid may be affected sometimes accompanied by swellings of salivary glands (uveoparotitis) Involvement of the bones of the hands or feet may cause absorption of bone and a radiographic picture of cyst like rarefactions Radiography may also show hilar glandular enlargement, radiating peribronchial infiltrations or a diffuse mottling

Course and Prognosis—Sarcoids may heal spontaneously or may steadily progress with increasing disability Sometimes tuberculosis develops the Mantoux reaction becomes positive and the sarcoid lesions disappear Some patients die from tuberculosis and some from right heart failure secondary to fibrosis of the pulmonary lesions others die from destruction of the bone marrow by sarcoid infiltrations

Diagnosis—Sarcoidosis has to be differentiated from perniones lupus vulgaris the deep and erythematous forms of lupus erythematosus tertiary syphilis leprosy drug granulomata and cutaneous reticuloses Reliance is placed on the morphology of the lesions the sarcoid histology, the negative Mantoux reaction the raised serum globulins and inverted albumin/globulin ratio, and X ray evidence of sarcoidosis in the bones or in the chest Radiographic findings in the lungs may suggest a diagnosis of tuberculosis pneumoconiosis or carcinomatosis The Kveim test is sometimes used This consists of the injection of an extract of proven sarcoid lymph nodes into the dermis Some 6 to 8 weeks later an indolent nodule develops which shows a typical sarcoid histology

Treatment—It is difficult to assess the value of treatment owing to the possibility of spontaneous remission A 3 months course of calciferol 150 000 units a day is worth a trial

The urine should be tested for albumin and the blood urea estimated periodically for evidence of toxicity from calciferol The skin lesions tend to improve more than the systemic ones with this treatment Isoniazid (300 to 400 mg daily) is worth a trial It has to be borne in mind that any treatment that hastens fibrosis of sarcoid lesions may in fact, shorten life by producing pulmonary fibrosis and right heart failure Intralesional injections of hydrocortisone (25 mg in 1 ml) at weekly intervals can be used to cause shrinkage and flattening of individual nodules if this is desired for cosmetic reasons or because of discomfort, as for example beneath spectacle frames

VIRUS INFECTIONS

HERPES SIMPLEX (RECURRENS) (FEBRILIS)

A malady, often recurrent consisting of outcrops of papulo vesicles which run their course in 10 to 14 days and end in scabs with minimal scarring

Clinical Picture—Without prodromal symptoms or with slight malaise the eruption begins with pink macules rapidly becoming vesicular The vesicles often show little or no erythema They may become slightly purulent or become broken and form blood scabs which detach in a few days leaving slightly depressed scars With the occurrence of further crops of lesions for the first few days of the illness all varieties of lesion—macules papules vesicles scabs and scars—can be seen in the one patient at the same time Itching is moderately severe In adults and sometimes in children there may be malaise and fever The distribution is widespread with involvement of the trunk more than the limbs also the scalp and the oral mucous membranes

Diagnosis is from papular urticaria in which the lesions appear mostly on the extensor surfaces of the limbs and consist of firm shotty itchy erythematous often golden scabbed papules sometimes much excoriated

From variola the diagnosis may be simple or extremely difficult Small pox in the unvaccinated is a malady with serious constitutional disturbance a heavy affection of the exposed parts marked sensitivity to light and all the lesions in the same stages of development but smallpox modified by vaccination and the milder variant of the malady known as alastrim may present with only one or a few lesions from which a diagnosis on clinical grounds may prove impossible Reliance must then be placed on virological and serological studies

Treatment—Varicella needs no treatment except rest in bed and calamine lotion with a normal or restricted diet depending on the presence or absence of fever

KAPOSI S VARICELLIFORM ERUPTION

This is a generalised infection with the virus of herpes simplex It occurs in infants with eczema who have been exposed to a sufferer from herpes simplex

Clinical Picture—There is a generalised eruption of varicelliform lesions high fever and general malaise

Course and Prognosis—There is a considerable mortality In those who survive the malady clears up in 2 to 3 weeks

Treatment—The best nursing is essential Secondary infection is common and possibly in part responsible for the mortality The use of antibiotics both systemically and locally is advisable The lesions should be dressed with bland applications such as calamine liniment

VACCINIA

Vaccinia is the result of deliberate or accidental inoculation with calf lymph The accidental form may follow deliberate vaccination and transference may take place on the same individual or to someone else The lesions are the same as those caused by vaccination in the susceptible and go through stages of erythema papulation vesiculation necrosis crusting and scarring The diagnosis is easy if the possibility is thought of and confirmed by enquiry

Individuals with Besnier s prurigo (atopic dermatitis) or infantile eczema are liable if accidentally or deliberately vaccinated to develop a generalised vaccinia with high fever and considerable malaise The condition has been called eczema vaccinatum and may be indistinguishable apart from the history and virological studies from Kaposi s varicelliform eruption due to the herpes virus Eczema vaccinatum may be further complicated by a severe coccal infection

Treatment—None is needed apart from protective dressings and topical antibiotics if secondary infection occurs Eczema vaccinatum needs rest in bed with good nursing and if secondary infection occurs appropriate antibiotics systemically and locally

skin, it may occur 10 to 14 days after exposure to varicella or varicella may follow at a similar interval after exposure to zoster

Histologically, there are intra epidermal mostly unilocular vesicles with swollen, grossly degenerate epidermal cells and an underlying inflammatory infiltrate proceeding to necrosis

Clinical Picture —There is a unilateral and segmental eruption consisting of grouped erythematous vesicles, with enlargement of the regional lymph nodes and a variable degree of pain in the area affected This pain may precede by a few hours the outcrop of vesicles It is severe in proportion to the patient s age being practically nonexistent in adolescents but often severe and persistent in the elderly Sometimes the pain develops its full intensity when the eruption is resolving and persists for months or years after the cutaneous manifestations have ended in scars This post herpetic neuralgia is most common in elderly patients

The lesions of zoster are at first erythematous then vesicular with erythematous margins The vesicles proceed to necrosis and dark crusts and secondary infection may then become superimposed When the scabs detach, depressed scars are left

Zoster is more serious in some sites than in others The first (ophthalmic) division of the fifth cranial nerve is often affected and the eye may then become involved with resultant opacity of the cornea and impaired vision or even with perforation of the cornea Involvement of the second division of the fifth cranial nerve causes palatal lesions in addition to those on the skin and involvement of the third division of this nerve produces lesions on the anterior two thirds of the tongue the floor of the mouth and buccal mucosa as well as on the chin When the seventh cranial nerve (geniculate ganglion) is affected there is pain and vesiculation on and behind the pinna the fauces and the posterior third of the tongue and, in addition facial palsy Involvement of the ninth cranial nerve (petrous ganglion) causes pharyngeal lesions

Course and Prognosis —Zoster once it has begun, inevitably proceeds through its various phases and ends with scarring in proportion to the intensity of the tissue reaction and amount of secondary infection in 2 or 3 weeks

Second attacks rarely if ever occur The prognosis as regards post herpetic pain is bad in direct proportion to the age of the patient

Treatment —There is no specific treatment for zoster The patient should rest in an equable temperature and a bland but not occlusive application should be applied such as calamine lotion or liniment Occlusive dressings encourage maceration and secondary infection of the lesions Suitable antibiotics locally applied are of value to control secondary infections but are no use for controlling the zoster itself For ocular involvement homatropin should be instilled and antibiotics used to control or prevent secondary infection For pain compound codeine tablets may be sufficient, or a preparation such as the following

Soluble phenobarbitone	gr ½
Tincture of gelsemium	m 10
Phenazone	gr 4
Syrup of lemon	dr ½
Peppermint water to	oz ½

½ fl oz t d s

For more severe pain, opiates may be necessary, particularly at night

VARICELLA (CHICKEN POX)

This is characterised by a polymorphic rash appearing in crops, with some constitutional disturbance and residual scarring

Ætiology —The virus is closely related if not identical to that of zoster The incubation period is 12 to 21 days

posterior pairs which bear trailing bristles The gravid female burrows in the horny layer where she deposits up to 30 eggs and then dies The larvæ hatching from the eggs have only two hind limbs until by repeated moulting they develop to mature males and females The larvæ and males burrow into hair follicles the males dying after impregnation of the females The complete life cycle takes 10 days Infection is by intimate skin contact the infestation is either a familial and household or a venereal complaint of bedfellows It may rarely spread by more casual contacts as in hand holding Itching begins about 3 weeks after infestation apparently due to the development of allergic hypersensitivity

Clinical Picture —Scabies may present as pruritus widespread eczema or in fected dermatitis urticaria impetigo or furunculosis Itching may be intolerable or inconspicuous depending on the integrity of the sensory tracts and on the mental alertness of the individual Thus in lepers imbeciles or in senile dementia there is no obvious discomfort from itching in individuals very heavily infested Secondary infection may then result in a picture re embling infective dermatitis or exfoliative dermatitis (Norwegian or crusted scabies) Nurses are very liable to become infested as a result of attending to these patients whose scales and even nails show an enormous acarine population

A history of familial incidence or of venereal exposure makes the diagnosis prob able In any widespread itchy eruption the physician should examine for scabies The sites involved and the presence of burrows should make the diagnosis clear Scabies affects thin skin areas below the collar line thus the anterior axillary folds the inner sides of the elbows the ulnar sides of the wrists and hands and the clefts of the fingers are sites commonly affected on the upper limbs On the trunk the sites most affected are the female breasts the abdomen male external genitalia and the buttocks and on the lower limbs the thighs ankles and feet in infants palms and soles are characteristically affected

The burrow is a linear slightly sinuous elevation in the skin at one end of which a darker speck marks the site of the parasite In cleanly individuals the burrows may be inconspicuous and it is best to search for them by oblique, almost tangential lighting in order to make minor elevations in the skin more obvious In less cleanly persons accumulations of dirt beside the burrows make their recognition easier Skin coloured or red follicular papules are also observed at the sites of election and elsewhere Both these types of lesion may be masked by scratching secondary infection or eczematous dermatitis In doubtful cases the diagnosis can often be made by finding adult parasites larvæ or ova This is best done by scraping open suspect burrow like lesions with a Harrison s scarifier through potassium hydroxide Microscopic examination may then reveal one or more of adult parasites, larvæ unhatched eggs or eggshell fragments

Scabies may be caught from cats and dogs but the parasites do not burrow there are only itchy papules and the disease dies out if the animal is avoided

Course and Prognosis —If untreated scabies infestations go on indefinitely *This is only likely to occur in individuals of low intelligence in whom itching may be* slight or absent By concurrent treatment of all members of the household scabies can be eliminated quickly, but if any one member of the household remains un treated or is treated at some other time recurrences are likely

Diagnosis is from pediculosis and from other causes of widespread itching eruptions associated with urticaria eczema dermatitis furunculosis and impetigo The manual lesions by themselves may suggest a contact dermatitis and a more general examination should be made in all such cases if there is the least cause for suspicion The diagnosis of scabies is made from a consideration of the history and the distribu tion and nature of the lesions and from microscopic examination Involvement of the penis and scrotum with itchy red papules is characteristic

Pediculosis corporis mostly affects the upper trunk and shoulders with scratch

WARTS (see Tumours of the Epidermis)

MOLLUSCUM CONTAGIOSUM (see Tumours of the Epidermis)

ORF (CONTAGIOUS PUSTULAR DERMATITIS OF SHEEP)

A virus infection resulting from the handling of infected sheep's heads

Ætiology—The malady may affect all handlers of sheep's heads and carcasses—shepherds, meat porters, butchers, cooks and housewives. The histological picture resembles that of cowpox, but virological studies differentiate the two conditions

Clinical Picture—The lesion usually occurs on a finger, on the hand or on the face as an œdematous inflammatory nodule. The inflammation attains its maximum intensity after 7 to 10 days, some central necrosis occurs, and the lesion gradually shrinks, disappearing after several weeks, leaving a scar. Constitutional symptoms are slight

Diagnosis is from vaccinia and milkers' nodes

Treatment—No treatment is effective in shortening the course. Topically applied antibiotics are helpful to control secondary infection

MILKERS' NODES

These are red nodules, occurring on the hands of milkers and probably due to the cowpox virus acting on someone with partial immunity. In the absence of such immunity, more typical cowpox develops, with bullous lesions on the hands or face

LYMPHOGRANULOMA VENEREUM VEL INGUINALE

This is a venereal disease caused by a virus

Clinical Picture—After an inoculation period of 7 days, a genital papule or vesicle or urethritis develops, followed in 2 weeks by enlargement of the inguinal lymph nodes which break through the skin with multiple sinuses. Involvement of the ano rectal glands from vaginal lesions may cause rectal stricture and genital elephantiasis. The infection may start as a proctitis

Diagnosis is from syphilis, soft sore, granuloma venereum and carcinoma of the rectum. The Frei test is positive

Treatment is by chlortetracycline or chloramphenicol, gr 3 every 8 hours for 14 days

GRANULOMA VENEREUM VEL INGUINALE

An infection with Donovani granulomatosis, mostly of coloured people, venereally acquired, of the anogenital region, causing nodules or vesico pustules, with slowly spreading ulceration and vegetations with serpiginous outlines and ending in extensive scarring. The Frei test is negative. *Donovania granulomatis* is responsible. The incubation is one or a few weeks

Diagnosis is from syphilitic, tuberculous and carcinomatous ulcers

Treatment is by antimony injections, streptomycin or chloramphenicol

PARASITIC INFESTATIONS

SCABIES

Scabies is an acarine parasitic infestation of the stratum corneum caused by *Sarcoptes* (*Acarus*) *scabiei*

Ætiology—The adult female is about 0 4 mm long, just visible to the naked eye, oval in shape, with two anterior pairs of limbs which bear suckers and two

individual without investigating home conditions with the aid of a health visitor All infested individuals should be treated concurrently

The hair is combed thoroughly with a fine mesh comb to unthread the nits (ova) by force In severe infestations it makes things easier if the hair is cut short. D D T application 2 per cent (B P C) is then rubbed into the scalp and not washed out for the next 24 hours the parasites are not killed immediately and may survive for a day or two or medicated (lethane) hair oil (N F) may be used in a similar way With either preparation a second application is made after an interval of 3 days Benzyl benzoate emulsion can also be used and is said to make it easier to remove the nits Lorexane a benzene hexachloride concentrate is also effective Any coccal infection that remains is dealt with afterwards by antibiotics Heat disinfestation of the bedding and headwear should be carried out

Prophylaxis —Of great importance in the prevention of scalp infestation is daily brushing and combing of the hair and a weekly shampoo This regime is often neglected when expensive permanent waving and setting is performed hence scalp infestation to day occurs mostly in young women apart from outbreaks in uncleanly families A low intelligence is common in adults with scalp infestation

PEDICULOSIS CORPORIS

The parasite is structurally similar to *P capitis* but slightly larger (4 mm long) *P corporis* is rare in peace time except among vagrants and inhabitants of common lodging houses In war conditions it tends to become more widespread

Clinical Picture —Itching of the body and scratch marks excoriations and patchy pigmentation with areas of eczematisation and lichenification sometimes with secondary infection suggest the diagnosis Exposed parts escape and the trunk is mostly affected especially the backs of the shoulders the waist and the buttocks and the proximal parts of the limbs The parasites visit the skin to feed and to deposit eggs on coarse hairs but spend most of their existence on the underclothing and bedding a completely different mode of life from sarcoptes Eggs are also affixed to fibres of textiles If the host is pyrexial the parasites move to the outer clothing and occasionally transference takes place of louse borne typhus in this way More common is transference from one person to another under overcrowded and un hygienic conditions

Course and Prognosis —Pediculosis is important not only in itself but also as the means of spread of more serious conditions such as typhus

Diagnosis is from scabies senile or general pruritus and dermatitis herpetiformis Scabies has a different distribution pathognomonic signs in the form of burrows and sarcoptes or ova may be found on scraping Senile pruritus may present with scratch marks and excoriations but parasites are not found on inspecting the clothing The physician must remember however that the patient may have put on clean underwear for his visit to the hospital Dermatitis herpetiformis affects the shoulder and pelvic girdles chiefly also the genitalia elbows and knees The physical signs are flaccid vesicles easily ruptured excoriations and patchy pigmentation There is a characteristic histology and a brisk response to treatment with sulphapyridine

Treatment —D D T powder (N F) 10 per cent liberally dusted on the patient s skin beneath the underwear is effective in controlling the personal infestation The underclothes and bedding should be heat disinfested and the seams of more super ficial garments run over with a hot iron

PHTHIRIASIS PUBIS

Phthiriasis pubis or crab louse infestation is usually acquired venereally *Phthirus pubis* is a short wide almost triangular louse 1 5 mm long and about the same width

marks, excoriations and patchy pigmentation *P capitis* may also cause scratch marks on the shoulders Parasites are found on the seams of underclothes and eggs on coarse body hairs or attached to underclothing

Treatment —The patient and all contacts must be treated concurrently Self treatment is difficult and the treatment of patients by each other is best In extensive family infestations and in epidemics or if home amenities are inadequate treatment at special cleansing stations is preferable

The full course of treatment takes 3 days On the first day the patient takes a warm bath and lathers and scrubs the body and limbs thoroughly all over with particular attention to the sites known to be most heavily involved After the bath the skin is not dried but benzyl benzoate 25 per cent is applied all over from the neck downwards using a paint brush 2 or 3 in wide Having made certain that every square inch of skin has been covered including the genitalia, perineum and toe clefts the patient dries in front of a fire puts on the previously worn nightwear and goes to bed between the previously used sheets On the second day the patient dresses in the previously worn underwear That day, a second application of benzyl benzoate is made but without a preceding bath then the patient dries before a fire and puts on clean underwear That night clean nightwear is worn and the patient goes to bed between clean sheets On the third day the patient takes a bath and the treatment is then at an end

If there is any further itching calamine lotion is applied and on no account must further applications of benzyl benzoate be made Patients sometimes give themselves repeated applications because itching often persists for a while after the two treatments and they interpret this as meaning that the infestation persists Repeated applications of benzyl benzoate may cause dermatitis medicamentosa For infants under 2 years of age, a half strength emulsion may be used Sulphur ointment (B P) (10 per cent for adults 2½ per cent for infants) may be used instead of benzyl benzoate emulsion but it is more liable to irritate the skin Underclothing nightwear and sheets are best dealt with by laundering and ironing Sarcoptes essentially lives on and in the epidermis and does not like the louse move away from the host hence it is unnecessary to disinfest bedding, blankets and the outer clothing

PEDICULOSIS

Three forms of lice live on man *Pediculus capitis* *Pediculus corporis* (*vestimenti*) and *Pediculus* (*phthirus*) *pubis*

PEDICULOSIS CAPITIS

Clinical Picture —The parasite is about 3 mm long with an oval head having two antennæ a powerful mandible and a proboscis The narrow thorax supports three pairs of legs each of which has a hook like extremity The abdomen is much wider than the thorax The eggs (nits) are laid on hairs being affixed by a cement like substance The larvæ hatch out from the egg by means of a movable lid *P capitis* may be asymptomatic and found during the course of routine examination of the scalp or it may present as itching of the scalp neck or shoulders with scratch marks, or as impetigo or pyoderma of the scalp On examination ova are found obliquely attached to hair shafts especially in the occipito parietal region In light infestations there may be eggs on a few hairs but in heavy infestations several eggs may be seen attached to one hair shaft The discovery of adult parasites on clinical examination is difficult except in heavy infestations Secondary infection causes matting of the hair an offensive odour pyoderma cervical lymphadenitis and sometimes œdema of the orbital tissues causing closure of the eyes

Treatment —Infestation may affect the family It is of no use treating the

themata may occur with or without fever they do not spread over the body surface in the same order as the exanthemata and some areas may escape In scarlatiniform toxic erythema the pattern may be coarse and the peeling more marked than in scarlatina but mouth lesions may be absent Milian s ninth day erythema is a scarlatiniform rash thought to be due to activation of a latent infection by a drug for example arsphenamine or sulphonamides The phenomenon is known as biotropism

Treatment is by finding and removing the cause Septic foci may need attention Often a cause cannot be found

FIXED ERYTHEMA

A localised and circumscribed recurrent erythema erupting in the same situation every time one particular drug is taken (see Drug Eruptions)

URTICARIA

A transient redness and swelling of the skin causing characteristic weals in the dermis or large hypodermal swellings

Ætiology —Urticaria is caused by dilatation of the capillaries and small arterioles and transudation therefrom Capillary dilatation may arise from the release of histamine or H substance and arteriolar dilatation from acetylcholine Urticaria may arise from external or internal causes The external causes include nettle stings (from their histamine and acetylcholine content) insect or jellyfish bites contact with woolly bear caterpillars or infestation with scabies In certain individuals friction causes wealing within a few seconds (dermographism or factitious urticaria) In such persons too scabies may present as urticaria In others heat is responsible and these persons also urticate from exertion or excitement (cholinergic urticaria) Urticaria from cold or from light (the yellow band of the spectrum) are both very rare Among internal causes are certain foods and drugs foci of infection intestinal parasites and hydatid cysts cutaneous reticuloses and emotional causes particularly resentment and masochism Urticaria may be dermal and present with itchy papules or with weals or it may be hypodermal and present with large non itchy swellings (giant urticaria angioneurotic œdema Quincke s œdema)

Clinical Picture —*Urticaria is conveniently divided on clinical grounds into* two forms acute or subacute single attacks and chronic or recurrent attacks

The acute form presents as itchy pink papules and weals—elevated pink areas with blanched centres brought about by the obliteration of the dermal vessels by the pressure of exudate The lesions appear suddenly with intense itching and disappear just as rapidly with the result that when the patient attends for examination physical signs may be absent Urticaria from the nettle may have pseudopodia apparently due to lymphatic spread of the injected histamine and acetylcholine Non itchy hypodermal skin coloured or pink swellings may also appear particularly around the eyes or mouth Swellings within the mouth are rare but potentially lethal at the back of the tongue or on the larynx, where they may cause obstruction of the respiratory tract The lesions may recur at intervals for a few hours or days and then cease Constitutional symptoms are usually slight or absent but the patient may be very anxious about the significance of the rash and depressed by the severe itching which interferes with sleep An emotional disturbance may lower the threshold of reaction to some antigen Sometimes a gastro intestinal disturbance precedes the eruption or foods such as shellfish or strawberries may have been eaten In other patients a drug is responsible usually aspirin a barbiturate halogen codeine phenolphthalein or quinine although many others can give the same effect. The injection of sera for example diphtheric antitoxin, or penicillin may be followed by urticaria within 10 to 14 days in the first instance or within a few hours after subsequent injections Acute local urticaria is usually caused by nettle stings mosquito bug or flea

with three pairs of legs having hook like ends Infestation may also take place in the axillæ on coarse body hairs and rarely on the eyebrows eyelashes or beard The brownish parasite hides in follicular orifices attached to hair shafts or suspends itself from two hairs and the females deposit ova on the hairs The bites of these parasites cause tiny blue spots known as 'maculæ cærulæ'

Clinical Picture —There is itching of the pubis and the sufferer often recognises the presence of the lice Bluish macules about 0 5 cm in diameter are observed but few if any, scratch marks can be seen

Treatment —Shaving the pubis is a great help Then D D T application medicated (lethane) hair oil, or benzyl benzoate application may be applied—all preferable to mercury ointment which often causes severe dermatitis Parasites on the eyelashes should be removed with forceps

INSECT BITES AND STINGS

The flea (human or dog) bed bug and gnat may cause urticarial papules with central puncta or large blisters may develop Bee wasp and ant stings may cause more violent allergic reactions in the susceptible individual

Treatment —Antihistamine creams may be applied and antihistaminic drugs taken by mouth A bee sting should be extracted if possible and weak ammonia applied Wasp and ant stings are also best treated with ammonia Dimethyl phthalate cream makes a useful repellent against gnats

ERYTHEMATOUS CONDITIONS

Erythema is a transient redness of the skin due to vasodilatation

SIMPLE ERYTHEMA

A transient redness of the skin from physical causes such as heat, cold and friction

INTERTRIGO

A shiny pink condition of opposing skin surfaces due to erosion of the superficial cells of the epidermis by mutual friction Secondary infection with monilia and cocci is common, giving rise to intertriginous (infective) dermatitis often with fissuring

Treatment of intertrigo is by suitable clothing uplift brassieres etc to prevent friction of the opposing surfaces and maceration from retention of sweat For simple intertrigo a dusting powder such as boracic talc powder is suitable If fungous infection is superimposed magenta paint is often helpful and if coccal infection develops the appropriate antibiotic Silver nitrate solution (2 per cent) is a useful application to fissures at the depths of the folds

TOXIC ERYTHEMA

A widespread reddening of the skin believed to be due to toxic agents of virus origin in measles and rubella of streptococcal origin in scarlatina due to drugs in morbilliform and scarlatiniform drug eruptions and some examples of urticaria erythema multiforme erythema nodosum etc or due to unknown causes

Diagnosis depends on a careful history and examination on the presence of fever coryza photophobia and Koplik s spots in measles occipital lymphadenopathy in rubella fever tachycardia headache vomiting circumoral pallor exfoliation of the tongue and sore throat in scarlatina drug eruptions and idiopathic toxic ery

themata may occur with or without fever they do not spread over the body surface in the same order as the exanthemata and some areas may escape In scarlatiniform toxic erythema the pattern may be coarse and the peeling more marked than in scarlatina but mouth lesions may be absent Milian s ninth day erythema is a scarlatiniform rash thought to be due to activation of a latent infection by a drug for example arsphenamine or sulphonamides The phenomenon is known as biotropism

Treatment is by finding and removing the cause Septic foci may need attention Often a cause cannot be found

FIXED ERYTHEMA

A localised and circumscribed recurrent erythema erupting in the same situation every time one particular drug is taken (see Drug Eruptions)

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bites, it may also occur around sites of injections Dermographism, too tends to be localised to sites where clothes rub or press

Chronic or recurrent urticaria presents as itchy papules and weals and subcutaneous swellings which usually occur more in the evening but sometimes in the morning Foods and drugs are seldom found to be responsible for this type of urticaria, and the most careful search for foci of infection or of infestation is often unrewarded with success Resentment fear or ungratified libido may precipitate the condition or cause exacerbation and fatigue is often the immediate precipitant

Diagnosis—The recognition of urticaria is usually easy even if there are no physical signs at the time of the examination the history of transient swellings perhaps with itching can only mean urticaria Dermatitis herpetiformis presents with vesicles excoriations crusts and pigmentation The lesions of erythema multiforme are more persistent than those of urticaria but less itchy

Giant urticaria is differentiated from erysipelas and contact eczematous dermatitis by the absence of fever and a dusky, brawny swelling which are found in erysipelas and by the absence of vesiculation and peeling which occur in eczematous dermatitis Discovery of the cause is another matter This is often simple in the acute form but in chronic cases it necessitates the most careful history and examination directed towards the discovery of allergens toxic foci infestations physical causes or faulty attitudes of mind Further, the urticarioid lesions of the reticuloses must be borne in mind and a white cell count is always advisable in the chronic form of the malady

Treatment consists of removal or avoidance of the cause and symptomatic relief by means of antihistaminic drugs while looking for the cause The patient should be instructed to stop taking any drugs that are not essential Suspected foods should be avoided and foci of infection treated Of the antihistaminic drugs promethazine hydrochloride 25 mg in the evening or twice a day, is perhaps most useful owing to its powerful soporific effect but sometimes this action is not desired and then mepyramine maleate 100 mg up to three times a day may be more suitable The dose of any antihistaminic drug should be adjusted so as to give the best control with a minimum of unwanted side effect the dose is reduced and the drug finally withdrawn as the symptoms are relieved This particularly applies to urticaria from injected drugs such as penicillin An aperient is sometimes useful In severe forms rest in bed is advisable

In the psychogenic variety, barbiturates or bromides may be as useful as antihistaminic drugs but if the urticaria is believed to have an allergenic basis it is wise to avoid all drugs except the antihistamines Relief of the psychogenic type depends on helping the patient to understand the significance of the symptom in relation to his attitude of mind Dextro amphetamine is a valuable sympathomimetic drug for these patients in a dose of 5 mg each morning Local treatment consists of calamine lotion, to which 1 per cent of phenol or 12½ per cent of weak lead subacetate solution may be added

LICHEN URTICATUS (PAPULAR URTICARIA)

This is a form of urticaria which occurs in children

Ætiology and Pathology—The malady tends to occur more in the summer months and may recur for several years The cause is unknown but something in the home environment is important it has repeatedly been shown that removal of the patient to hospital without any other alteration in treatment may bring about a prompt remission Insect bites are responsible in a proportion of cases but in many patients a tense emotional environment seems to be another important factor

Histologically there is acanthosis spongiosis and œdema with a chronic infiltrate around the vessels of the dermis

Clinical Picture—Itchy pink or skin coloured shotty papules appear in crops mostly on the extensor surfaces of the limbs but also on the buttocks and trunk The papules soon acquire vesicular tops which may become crusted and excoriated

Course and Prognosis—The malady may persist for several weeks

Diagnosis is from scabies varicella and insect bites Scabies affects the flexor surfaces and the elementary lesions are burrows and follicular papules Penile scrotal and mammary lesions are characteristic The history may reveal other cases in the family Varicella presents with a polymorphic eruption of macules papules, vesicles and crusts The scalp is often affected and the trunk more than the limbs There are often vesicles on the buccal mucosa Insect bites may show puncta or there may be large bullæ on the legs but papular urticaria may sometimes be a generalised reaction of hypersensitivity to insect bites and puncta will not then be seen

Treatment—Any drugs being taken should be withheld and careful enquiry should be made into the child s diet with particular reference to fruits and sweets Any imbalance or excess should be adjusted An examination at the home may reveal bug infestation or flea infested animals Antihistaminic drugs in syrup form are useful for example elixir Benadryl 1 to 2 dr or elixir Phenergan in a similar dosage Removal of the child into hospital may succeed after all else has failed

URTICARIA PIGMENTOSA (XANTHELASMOIDEA)

A pigmented macular eruption with urtication

Ætiology and Pathology—The cause is unknown

Histologically there are numerous mast cells in the upper dermis in the infantile form but few or none in the adult form

Clinical Picture—In the first year of life brown macules urticarial papules and small weals are seen The lesions appear anywhere on the skin in crops each lesion starting as a papule or weal and proceeding to pigmentation The pigmented macules urticate on friction Weber has described a form in which there are telangi ectatic red macules with very slight pigmentation

Course and Prognosis—In the infantile form the lesions may disappear after several years In the adult form they are said to be more persistent and the telangi ectatic form may end fatally as a mast cell reticulosis

Diagnosis from papular urticaria in infancy is by the marked pigmentation and the presence of mast cells in the dermis The adult form may be mistaken for secondary syphilis but is recognisable by the urtication

Treatment is symptomatic by calamine lotion and a trial of antihistaminic drugs

ERYTHEMA MULTIFORME

An eruption with a marked tendency to recurrence of well defined reddened areas of skin which mostly appear on the extremities

Ætiology and Pathology—Erythema multiforme is a reaction of hypersensitivity to a variety of known or suspected causes in particular bacterial and virus infections and drug intoxications It is characteristically recurrent and is sometimes preceded by herpes simplex It is a rare complication of the X ray treatment of Hodgkin s disease

Histologically there is dilatation of the dermal blood vessels with a cellular mainly lymphocytic infiltrate around them and some serous exudation There may be some spongiosis

Clinical Picture—Erythema multiforme usually affects young adults There is no obvious seasonal incidence but a marked tendency to recurrence The distal parts of the limbs and the face are most affected and often the vermilion and mucous surfaces of the lips and the mucosæ of the mouth and genitalia are also involved

bites, it may also occur around sites of injections Dermographism too tends to be *localised to sites where clothes rub or press*

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and erythema figuratum perstans (Wende) are generally regarded as closely related if not identical

In this malady there are large annular and polycyclic pinkish grey lesions with slightly scaly borders usually with a free edge centripetally The lesions may slowly extend in one direction and fade out in another

Treatment —In some cases Fowler s solution has been reported to bring about *a remission Apart from this only symptomatic measures can be employed*

PURPURA

Purpura or the extravasation of blood in the skin may be due to many causes one of three pathological abnormalities is usually responsible There may be a defect in the vessel walls due to bacterial or chemical toxins or malnutrition there may be a deficiency of platelets or some defect in the complex process of clotting or there may be an increase of capillary pressure

In the first group is purpura in meningococcal septicæmia or in subacute bacterial endocarditis also the purpura of fulminating exanthemata—scarlet fever measles smallpox typhus etc Certain drugs for example iodides barbiturates sulphonamides may cause purpura The purpura of scurvy is due to a deficiency of the ground substance between the endothelial cells Schoenlein Henoch s purpura or allergic purpura is thought to be brought about by damage to the endothelial cells by circulating antigens

In thrombocytopenic purpura the absence of thrombocytic plugs to fill any gaps in mildly traumatised cutaneous vessels is responsible for the purpura

Purpura may also arise on the legs from hypostasis and in widespread eczematous conditions it is not unusual to see a purpuric component to the lesions on the lower extremities while those on the upper extremities show eczematous features only

Diagnosis —Purpura is differentiated from erythematous lesions by the persistence of the dark red colour on diascopy—examination through a glass spatula slide or watch glass with which pressure is applied so as to expel blood from the vessels

Discovery of the cause of the purpura depends on a full and careful clinical investigation with particular attention to the diet drugs fever enlargement of the spleen and manifestations of non cutaneous allergy or purpura such as joint swellings hæmaturia intestinal colic etc A full blood and platelet count is essential and an estimation of the clotting and bleeding times In the rare cryoglobulinæmic purpura the plasma undergoes gelification at room temperatures It chiefly affects exposed parts

Treatment is of the cause (This subject is dealt with more fully elsewhere)

THE TOXIC CAPILLAROSES

In addition to frank purpura the skin may be affected by pigmentary and telangiectatic conditions which have been given various clinical descriptions but which all show a similar histological picture suggesting some damage to the endothelium of the vessels

Ætiology and Pathology —In all types the cause is unknown

The histological picture is one of dilatation of superficial capillaries with intimal proliferation and degeneration and a perivascular infiltrate Extravasated blood cells may be seen and depositions of hæmosiderin There may be some epidermal atrophy

Clinical Picture —This varies according to the type of capillarosis

In Majocchi s disease (purpura annularis telangiectodes) the patients are usually young women and the eruption consists of discs or rings of telangiectasia with brown discolouration due to slight extravasations of blood The lesions form on the thighs or legs and very slowly extend peripherally and heal centrally with a slight residuum of atrophy

Lesions on the trunk are relatively rare An attack may be ushered in by malaise for 48 hours before the characteristic outbreak

The lesions are polymorphic and maculo erythematous papulo vesicular bullous and hæmorrhagic varieties occur They persist in one situation throughout an attack and do not show the evanescent properties of urticaria The central part of the lesions may be paler or darker than the periphery, the former indicates early bulla formation the latter is due to hæmorrhage or to brown pigmentation In either case the picture of erythema iris results

When the exudate in these cutaneous lesions has been absorbed they take on a dry, superficial fissured and scaly brownish red discoloration followed by peeling and resolution The mucosal orogenital lesions differ from those of the skin in that erosion occurs more easily with the result that a moist ulcerative pseudomembranous condition results along the vermilion surface of the lips in the mouth or on the glans penis or mucosa of the vulva There may also be pain and swelling of joints fever and albuminuria but usually subjective symptoms including itching are slight.

The Stevens Johnson syndrome is a severe variant of erythema multiforme with exudative bullous and erosive cutaneous lesions extensive and distressing involvement of the mouth and lesions on the conjunctiva and cornea of the eye which may go on to pannus and blindness This malady is accompanied by fever and malaise

Course and Prognosis —Attacks of erythema multiforme usually clear spontaneously after 2 or 3 weeks but recurrences after intervals of months or years are common The common form leaves no sequelæ but the severe form may lead to dimness of vision or blindness

Diagnosis is from other bullous conditions on the hands and elsewhere and from other erythematous conditions Thus pompholyx dermatitis herpetiformis pemphigus and pemphigoid lupus erythematosus and urticaria may all at one time or another have to be excluded Pompholyx may present with large bullae but there is no marked erythematous component unless secondary infection occurs Dermatitis herpetiformis presents with intensely itchy vesicular and eroded lesions on the shoulders buttocks elbows, knees or elsewhere but there is little or no erythematous halo to the lesions In pemphigus the bullæ are flaccid and extend when lateral pressure is applied to them (Nikolsky s sign) They may arise from normal coloured skin In pemphigoid the bullæ are tense but Nikolsky s sign is positive There may be pink areas around the bullæ This malady may in fact so closely conform to the clinical and histological pattern of erythema multiforme as to be regarded as senile erythema multiforme perstans Subacute and cutaneously disseminated lupus erythematosus may resemble erythema multiforme but the distribution is more on the face and upper part of the chest In doubtful cases a raised erythrocyte sedimentation rate leucopenia and increased serum globulins will support the diagnosis of lupus erythematosus Urticaria is characterised by the short lived and recurrent nature of its lesions which come and go first at one site then at another

Treatment is supportive by rest (in bed in severe forms) and bland local applications such as calamine lotion or Lassar s paste Internally antihistaminic drugs such as mepyramine maleate or promethazine hydrochloride may prove helpful In the severe Stevens Johnson form active measures must be taken to avert the serious eye conditions that can result The administration of corticotrophin is an urgent measure to help the patient through the severest phase A dose of 50 mg every 6 hours is advisable for 4 days after which the drug is gradually withdrawn

ERYTHEMA ANNULARE CENTRIFUGUM (DARIER)

This is believed to be a variant of erythema multiforme though some examples have seemed to be more akin to dermatitis herpetiformis The conditions called erythema simplex gyratum (Jadassohn) erythema chronicum migrans (Lipschutz)

on perniotic legs of young women Ulceration is common with considerable scarring and disfigurement In some cases the differential diagnosis may prove impossible except after a period of observation

In erythema induratum (Whitfield) (*q v*) the patients are *usually women* between 30 and 45 years of age This malady sometimes called nodular vasculitis is probably a variant of erythema nodosum but the lesions which come out in crops are more persistent than those of erythema nodosum and leave discoloured hard areas in the skin Ulceration is uncommon In periarteritis nodosa the lesions are more persistent and necrotic and they may appear anywhere on the body or limbs

Treatment —The patient should be kept in bed until the nodules have subsided Chemotherapeutic and antibiotic drugs are best withheld because their administration may be followed by an exacerbation of the skin condition Symptomatic treatment is best with the minimum use of drugs of all kinds excepting aspirin which may be given with benefit Vitamin supplements an adequate diet and subsequently a period of convalescence and return to good housing conditions are desirable A bland local application for example calamine lotion or titanium dioxide paste is *suitable*

If the Mantoux reaction is undergoing or has recently undergone conversion it is important that the patient should not come into contact with tuberculous individuals except inadvertently and unavoidably for some months at least If the patient is a nurse she should not be allowed even after convalescence to take up nursing of tuberculous patients Every patient with erythema nodosum should be investigated by clinical and radiographic means for evidence of tuberculosis elsewhere

ERYTHEMA INDURATUM

This is of three types erythema induratum of Bazin a subcutaneous tuberculide the subcutaneous sarcoid of Darier Roussy and erythema induratum of Whitfield (nodular vasculitis)

BAZIN S DISEASE

This affects the unshapely calves of young women with perniosis It is believed to be a tuberculide localised to the calves because of the defective circulation (see p 1244)

DARIÉR-ROUSSY SUBCUTANEOUS SARCOID

This is similar to Bazin s disease in appearance but does not ulcerate The Mantoux reaction is negative there is a sarcoid histology and the condition reacts sluggishly if at all to antituberculous drugs (see p 1246)

ERYTHEMA INDURATUM OF WHITFIELD (NODULAR VASCULITIS)

This presents as recurring tender hard subcutaneous nodules in the legs of women of 30 to 45 years of age The condition is not a tuberculide but is a variant of erythema nodosum possibly of streptococcal origin There is no specific treatment, elastic supports often give relief

LUPUS ERYTHEMATOSUS

An erythematous and atrophic malady presenting in two forms the first circumscribed benign cutaneous and chronic the second malign systemic and acute An intermediate form occurs—chronic or subacute disseminated lupus erythematosus

CHRONIC DISCOID LUPUS ERYTHEMATOSUS

Ætiology and Pathology —The cause is unknown

The characteristic features of the histology include in the chronic discoid variety

In Schamberg's disease (progressive pigmentary dermatosis) men are usually affected on the legs more often than elsewhere but sometimes at sites of pressure Dark reddish brown puncta the 'cayenne pepper' spots are visible in a zone of brownish skin The lesions may itch and they slowly enlarge but may ultimately resolve spontaneously, leaving some pigmentation A similar condition is sometimes seen on the legs of patients with varicosities

The pigmented lichenoid purpuric dermatitis of Gougerot and Blum presents with discrete and agglomerated papules, with petechiæ pigmentation and telangi ectasia The lesions may appear on the trunk or on the limbs

Angioma serpiginosum (Hutchinson) presents with telangiectasia which by clear ance at one site and spread at another comes to acquire an annular or a serpiginous arrangement The body or limbs may be affected

Treatment—As no cause is at present known for these conditions, none other than supportive treatment can be offered The patient should be investigated for foci of infection, diabetes and vascular hypertension

OTHER FORMS OF CAPILLAROSIS

Occasionally extensive eruptions of capillarosis are seen on the lower extremities buttocks, trunk, shoulders, elbows and elsewhere of young men It has been shown in some cases that textiles are responsible but the exact cause whether it be dye mordant or something else, has not yet been determined The eruption usually persists for several months No treatment is effective in bringing about earlier remission

ERYTHEMA NODOSUM

This is an outbreak of tender nodules on the legs and sometimes on the forearms which in their healing stage have the appearance of bruises (erythema contusiforme)

Ætiology and Pathology—The cause is a reaction of hypersensitivity in the subcutaneous vessels of the limbs which bring about an inflammatory reaction in and around the vessel walls (nodular vasculitis) The sensitising causes include tubercle bacilli, streptococci and occasionally meningococcal and other infections In the United States a common cause is coccidioidomycosis The lesions may also develop when chemotherapeutic and antibiotic drugs release organismal products to which the patient is sensitised

Histologically there is a focal dense infiltrate of neutrophil leucocytes and lympho cytes in the more superficial hypoderm The infiltrate invades the vessel walls (venules) and there is endothelial proliferation and thrombosis

Clinical Picture—Often after a sore throat or an upper respiratory infection the patient usually a child or young adult complains of tender swellings on the fronts of the legs and perhaps on the forearms The lesions are at first red and later brownish blue or even greenish, obtuse nodes with somewhat ill defined limits There may be a dozen or more lesions on the two limbs The natural course of the lesions is to undergo slow resolution disappearing in a few weeks without visible permanent change The nodules do not break down (except a rare form occurring with severe exacerbations of ulcerative colitis)

Course and Prognosis—Erythema nodosum clears spontaneously after a few weeks The lesions in themselves are of no import but they are of great significance in that they may indicate the presence of a primary tuberculous infection with hyper sensitivity Other manifestations of tuberculosis may follow and every patient with erythema nodosum should be kept under periodic observation for some months In cases due to hypersensitivity to streptococci the prognosis is better The erythrocyte sedimentation rate is a useful guide in following the progress of erythema nodosum

Diagnosis is from erythema induratum (Bazin) erythema induratum (Whitfield) and periarteritis nodosa In the first named the lesions are larger and usually arise

Treatment —When the clinical diagnosis of lupus erythematosus has been made it is wise to have the erythrocyte sedimentation rate estimated because if this is within normal limits it is most probable that the condition is in fact the benign cutaneous form of the malady but if the erythrocyte sedimentation rate is increased and particularly if there is also leucopenia the condition is probably systematised and potentially malign no matter how benign the cutaneous manifestations may seem to be An estimation of the serum protein may then reveal an increase of globulins and an albumin/globulin ratio of less than unity

The treatment of discoid lupus erythematosus is in the present state of knowledge empirical and the clinician can only treat every case on its merits giving whatever remedy in his experience produces the best results

Mepacrine 0 1 g up to three times a day is successful in many cases in bringing about a remission It should be taken until the lesions fade or until the skin becomes yellow whichever is the sooner and then the dose is gradually reduced a course lasting anything up to 3 months Periodic urinary examinations are a sensible pre caution and the patient should be examined at regular intervals so that the drug can be withdrawn at once should a toxic eruption begin to show itself Alternative oral remedies include mercury with potassium iodide and quinine Sulphonamides are contraindicated Vitamin supplements may be indicated and crude liver injec tions sometimes bring about relief Isoniazid has not been found of value in lupus erythematosus

Another valuable treatment in some cases is weekly injections of bismuth oxy chloride 0 2 g in 1 ml intramuscularly into the upper quadrant of the buttock the course extending up to 8 or 12 injections Injections of gold (sodium aurothiomalate) have been advocated but the risks of gold dermatitis are too considerable to justify the use of this remedy except for some very good reason If used the dosage should be low (10 to 25 mg) the urine should be tested and the body surface inspected before each injection and the course should comprise a total dosage of not more than 250 mg in about 12 weeks The drug is cumulative

Local treatment is also of great importance and value Local applications have no healing action but they can protect the lesions from mechanical injury screen them from light and provide cosmetic camouflage Titanium dioxide paste can fulfil all these functions or the patient may prefer the more æsthetic make up preparations of the cosmetic firms As an ultra violet screening cream salol 10 per cent or para aminobenzoic acid 15 per cent can be incorporated in a vanishing cream base but must be reapplied frequently if sweating is heavy

Local therapeutic practices include applications of carbon dioxide snow (—78 C) or slush the former being compressed into a pencil and applied for about 10 seconds to thickened red areas and the latter made by adding acetone to carbon dioxide snow and then applying it for one or two brief freezes by means of a camel hair brush or cotton wool on a probe The aim is to bring about an inflammatory reaction which will be followed by the formation of smooth and supple scarring Snow has a deeper action than slush and is more suitable for localised thickened lesions

Contraindicated in lupus erythematosus are sulphonamides by mouth and ultra violet irradiation X rays or radium locally the former because an exacerbation may result the latter because exacerbation or even malignant changes (epithelioma) may be initiated by these means

SYSTEMATISED LUPUS ERYTHEMATOSUS

Ætiology —The cause is unknown Over 90 per cent. of cases occur in women usually between the ages of 20 and 40 The disease may arise in a patient with chronic discoid lupus erythematosus or it may follow exposure to sunlight or the exhibition of drugs such as sulphonamides iodides thiourea and organic arsenicals

hyperkeratosis with keratotic follicular plugging, atrophy of the prickle cell layers liquefactive degeneration of the basal cell layer and basophilic degeneration of the collagen and elastic tissue, with a lymphocytic infiltrate mainly distributed around the vessels and cutaneous appendages

Clinical Picture —This form affects the face particularly across the nose and malar ridges (bat s wing lupus), also on the forehead, chin lower lip and ears Young and middle aged women are more often affected than men, and the condition is not seen in children The lesions are well defined, red rings, ovals or irregular shapes with marked thickening peripherally and paler atrophic centres On the surf ce are white or grey closely adherent scales, and horny plugs may be visible in the ostia of the follicles The patches remain stationary or slowly extend at one site while atrophic scarring develops at another Other sites characteristically affected include the vertex of the scalp (scarring baldness with redness and follicular plugging) the mucosæ of the cheeks (leucoplakia and reddened areas with erosions), the hands (red, scaly thickened patches on the backs of the fingers between the joints chilblain like redness around the nail folds, lupus pernio of Hutchinson) and the arms and upper part of the trunk In chronic or subacute disseminated lupus erythematosus many of these sites may be affected in the one patient

Course and Prognosis —In patients in whom the diagnosis of chronic discoid lupus erythematosus is firmly established by pathological as well as clinical means the course is usually of intermittent clearance and relapses on the skin with on the whole a gradual extension Sometimes the disease becomes inactive and scarring alone remains Transition from the chronic discoid to the acute systematised form rarely occurs but there are examples of the systematised form which present with lesions apparently so benign and chronic that the incorrect diagnosis of the chronic discoid form is made unless examination of the blood is carried out

Diagnosis is from lupus vulgaris and other granulomatous processes from carcinoma cutaneous reticulosis rosacea and light sensitisation dermatitis

Lupus vulgaris usually begins in childhood lupus erythematosus in adult life Lupus vulgaris shows translucent yellowish nodules which may be scattered around the edge of the scarred area, lupus erythematosus is characteristically a centrifugal process with adherent scaling and central atrophic scarring Lupus vulgaris may destroy the cartilage of nose or ears and cause great disfigurement Lupus erythematosus does not affect cartilage but is confined to the skin

Syphilitic gummata characteristically break out on the surface following the destruction of cartilage and bone, but they may also present as infiltrated irregular, soft reddish brown nodulations Psoriasis of the face may resemble lupus erythematosus but the scales are white, mica like and easily detached and typical psoriatic lesions are present elsewhere Seborrhœic dermatitis causes greasy scaling on a reddened background but the lesions itch and are more numerous and less well defined than in lupus erythematosus Sarcoidosis nodules more closely resemble lupus vulgaris but may mimic lupus erythematosis profundus In these circumstances biopsy is essential Lymphomata (Spiegler-Fendt sarcoids) are dome shaped dusky nodules with little or no epidermal change

Lupus erythematosus on the alæ nasi may resemble carcinoma cutis The redness may be slight, the border markedly raised the centre ulcerated, but follicular plugging is present and there is no pearly edge If the diagnosis cannot be established on clinical grounds alone biopsy will decide it One form of lupus erythematosus resembles rosacea in distribution but the lesions are persistent and associated with some degree of atrophy and there is no vasolability Light sensitisation dermatitis may resemble the less infiltrated form of lupus erythematosus but the lesions are more diffuse eczematised and itchy Chilblains on the fingers resemble lupus erythematosus but they only occur with cold weather, whereas lupus erythematosus persists throughout the year

ised lupus erythematosis must be considered in all cases of inexplicable pyrexia or when there is wasting anæmia, albuminuria purpura or lymphadenopathy also in the presence of acute neurological episodes The diagnosis is confirmed by the presence of a raised blood sedimentation rate leucopenia hyperglobulinæmia album inuria and the discovery of the L E cell

Treatment—Corticotrophin or cortisone may bring about a remission and pre vent relapse The effect on the ultimate prognosis is less favourable although a few apparent cures have been reported An initial dose of 50 mg of corticotrophin intra muscularly 6 or 8 hourly should be given and gradually reduced Renal involvement is a contraindication as renal failure may be precipitated presumably due to ischæmic changes following healing of the arterial lesions

The patient with chronic discoid lupus erythematosus and laboratory evidence of systematised lupus erythematosus should avoid sunlight extremes of temperature and the drugs mentioned previously

DRUG ERUPTIONS (DERMATITIS MEDICAMENTOSA)

Almost any drug may cause a skin eruption at one time or another but some drugs have this property to a much greater extent than others and certain individuals are unduly susceptible to drugs Drugs may produce ill effects from their external or from their internal use in several ways

External use Drugs applied externally may give rise to toxic effects in the following ways—(*a*) Contact eczematous dermatitis as from the topical use of sulphona mides antibiotics surface anæsthetics antiseptics antihistaminics etc (*b*) Light sensitisation as from sulphonamides tar quinine etc (*c*) Toxic effects on various organs after absorption as from sulphonamides flavine mercury (liver kidney) resorcin (thyroid) etc

Internal use Drugs taken internally may cause toxic effects by—(*a*) Toxic action on the skin immediate or accumulative (*b*) Induction of allergic hypersensitivity in the cutaneous vessels (*c*) Toxic action on bone marrow liver kidneys thermo static centre etc causing purpura skin infections nutritional deficiency hæmaturia albuminuria fever etc (*d*) Indirect toxic or allergic action through the destruction of bacteria and the release of their toxins (*e*) Destruction of organisms capable of synthesising vitamin B in the gut (*f*) Interference with absorption from the gut (*g*) Destruction of competitors of monilia in the gut (*h*) By competing for enzymes that are essential for cellular welfare (*i*) Aggravation of a pre existing dermatosis (*j*) Activation of virus infections herpes simplex zoster

Drug eruptions may also be of mixed external and internal origin A drug (for example penicillin sulphonamide) may be used topically in the first instance and cause an eruption from its subsequent internal use or it may be used internally in the first instance and cause an eruption when it is subsequently used by local application

Clinical Pictures—Many drugs cause nonspecific eruptions and a few have specific effects

The nonspecific eruptions in their simplest forms are morbilliform and scarlatini form erythemata In greater degrees of intensity there may be a resemblance to erythema multiforme with or without bulla formation or the toxic action on the bone marrow or cutaneous blood vessels may be sufficient to cause purpura Urticaria implies vascular hypersensitivity More specific effects include fixed erythemata pruritus exfoliative dermatitis pigmentation eczematoid psoriasiform acneiform lichenoid seborrhœic or pityriasis rosea like eruptions granulomata stomatitis and urethritis Usually there is something atypical about the eruption that differentiates

Pathology —The commonest findings at necropsy are chronic obliterative pleurisy pericarditis, perihepatitis and perisplenitis There are small warty endocardial vegetations in one third of the cases

Histological examination shows proliferation and fibrinoid degeneration of collagen in the supporting tissues of the serosal surfaces, myocardium, mediastinum retro peritoneal tissues and skin There is fibrinoid degeneration and necrosis of the connective tissue of the media of small arteries and arterioles, with proliferation of the endothelium, sometimes leading to thrombotic occlusion of the vessel these changes are usually found in the kidney, spleen and skin

In the kidney there may be focal necroses of capillary loops and the basement membrane of glomerular capillaries may be thickened and eosinophilous In the spleen the central artery of the Malpighian bodies may be surrounded by concentric rings of connective tissue

Clinical Picture —The manifestations of the disease are those of a febrile, wasting illness with inflammation of serous membranes depression of the bone marrow and finally, symptoms of vascular changes in viscera, especially the skin and kidney

The joints are frequently affected usually with a slowly shifting polyarthritis There may be swelling of the joints but permanent deformity is uncommon Pleurisy with effusion and pericardial effusion occur Hypertension is uncommon but albuminuria and microscopic hæmaturia are frequent The spleen and lymph glands may be enlarged anæmia is common and purpura may be found Diarrhœa is the commonest gastro intestinal symptom, and there may be vomiting abdominal pain and jaundice Mental changes are common, they vary from anxiety to toxic confusional states and delirium Involvement of the nervous system may cause epilepsy and rarely lymphocytic meningitis, encephalomyelitis or peripheral neuritis Examination of the fundus oculi may show hæmorrhages exudates and papillœdema Cutaneous manifestations may be marked slight or absent temporary or persistent On the face and chest there may be erythematous patches resembling erythema multiforme There may be red petechiæ or telangiectases on the tips of the fingers splinter hæmorrhages under the nails and a condition resembling chilblains on the fingers The palms may show ill defined erythematous blotches There may be redness and leucoplakic changes in the mouth on the lips or in the ano genital region

Laboratory findings include an increased red cell sedimentation rate leucopenia and the discovery of the L E cell on mixing the patient s plasma with her own or someone else s blood cells This cell is a polymorphonuclear leucocyte which has ingested degenerate nucleoprotein material and it is rarely seen except in systematised lupus erythematosus

Course and Prognosis —The course varies considerably The illness may be acute and fulminating from the beginning with high remittent fever prostration and joint pains, alternatively there may be acute exacerbations in a subacute or chronic form of the disease which may be precipitated by exposure to sunlight or exhibition of the drugs previously mentioned Death may occur in a few weeks The disease more usually runs a subacute course of many months or a chronic course of 5 or even 10 years Relapses and remissions are common the remissions rarely lasting longer than a year Death is usual within 5 years Spontaneous cure of the disease has been described but must be very rare Patients are often seen with chronic discoid lupus erythematosus who have a raised blood sedimentation rate leucopenia and hyperglobulinæmia who nevertheless continue in a reasonable state of well being the number of these patients who develop the florid manifestations of systematised lupus erythematosus is unknown but the long term prognosis is unfavourable

Diagnosis —The facial lesions may resemble erysipelas erythema multiforme or dermatomyositis When the joint manifestations are prominent the disease will have to be differentiated from acute rheumatism and rheumatoid arthritis Systemat

Psoriasiform arsenic gold mepacrine
Purpura antihistamines arsenic aspirin barbiturates carbromal chloral hydrate halogens mercury penicillin phenazone phenytoin Pyramidon quinidine quinine salicylates Sedormid sera sodium aminosalicylate sulphonal sulphonamides
Stomatitis antibiotics arsenic barbiturates bismuth gold halogens mercury phenacetin phenazone phenobarbitone phenolphthalein quinine, salicylates sulphonamides
Tuberculides (exacerbation) calciferol
Urticaria most of the drugs in this list arsenic aspirin barbiturates bromides cocaine derivatives iodides penicillin phenacetin phenolphthalein quinine sera and sulphonamides are common causes
Vesiculation (varioliform) halogens sulphonamides
Zoster arsenic

Course and Prognosis—Many eruptions are transient clearing rapidly after withdrawal of the drug but penicillin urticaria may persist for several weeks and halogen eruptions may continue to worsen after the drug has been withdrawn Some injected drugs for example gold are cumulative in their effects and dermatoses caused by them often worsen steadily after the last injection Inorganic arsenic has delayed effects the first signs appearing some years after the drug is first taken possibly even several years after its use has been abandoned

The prognosis depends on the possibilities of bringing about elimination of the drug and on the presence or absence of toxic effects on the liver kidneys and bone marrow

Diagnosis—The possibility of drug causation or aggravation has to be borne in mind in many dermatoses particularly if there is something atypical in the eruption and questioning has to be directed accordingly Analgesics aperients hypnotics sedatives and antibiotics are particularly suspect Withdrawal of a suspected drug may be followed by immediate improvement With nonspecific eruptions and when the patient has been taking more than one drug a test dose is justifiable This should only be given when the dermatosis has subsided and one tenth of the previous therapeutic dosage should be given in the first instance because if the full dose is given an unnecessarily violent reaction may result

Prevention and Treatment—The history may indicate sensitivity to one or more drugs Some drug eruptions result from neglecting to enquire into this possibility Potent drugs are sometimes used without sufficient justification In every case it is a useful self discipline to ask oneself Do the advantages likely to be obtained by giving this drug outweigh its possible ill effects? Whenever there is a choice a drug of lesser toxicity and sensitising potential should be used Especial care is necessary when there is albuminuria

To make treatment easier it is as well to tell the patient of possible side effects of a drug This encourages discontinuation of the drug immediately untoward symptoms develop and prevents further toxicity For most drug eruptions withdrawal of the drug is all the treatment that is necessary or in fact possible An aperient or an enema is sometimes useful when there is reason to think that some of the drug remains in the bowel Specific treatments are indicated in a few conditions For halogen eruptions sodium chloride or ammonium chloride may be given in a dose of 5 to 10 g daily In severe cases with toxæmia intravenous normal saline infusions should be given daily 100 ml on each occasion for a week

Heavy metal intoxications (gold bismuth mercury) are treated with dimercaprol (B A L) 2 ml 4 hourly gradually reduced to 2 ml daily in courses lasting a week with a week of intramuscular crude liver extract interposed The pigmentation of argyria is permanent The effects of inorganic arsenic (raindrop pigmentation keratoses carcinomata, hepatitis) are irreversible The keratoses are best treated with

it from the disease it mimics but this is not always so the lichenoid eruption due to mepacrine sometimes being identical to "idiopathic lichen planus possibly because it is in fact, lichen planus, triggered off by the drug Many toxic eruptions remain unexplained on a drug basis Sometimes this is due to drug contamination of foods for example the use of phenolphthalein to tint icing pink and the possibility of other food "processings" being the cause of toxic eruptions is a matter for speculation

The more common manifestations and some of the drugs that may cause them include

- Acneiform pustular bromides, corticotrophin, iodides sometimes sulphonamides
- Albuminuria bismuth, calciferol gold mercury, sulphonamides sera.
- Alopecia (cicatricial) gold mepacrine
- Bullous (pemphigoid) barbiturates, chloral, cinchophen, dapsone, halogens phenazone, phenolphthalein, phenytoin, quinine, salicylates streptomycin sulphonamides
- Coryza arsenic, iodides salicylates sulphonamides
- Cyanosis phenacetin sulphonamides
- Eczematoid antihistamines, arsenic, gold halogens, mepacrine, mercury, penicillin quinine sulphonamides
- Erythemata, morbilliform and scarlatiniform most of the drugs mentioned elsewhere in this list also atropine, belladonna, digitalis ephedrine, insulin, ipecacuanha, phenylbutazone procaine, rhubarb santonin turpentine
- Erythema multiforme like acetanilide, barbiturates, bismuth, dapsone, gold quinine sera sulphonamides thiouracil
- Erythema, fixed (localised and recurrent) phenolphthalein most commonly, also reported from arsenic, amidopyrine barbiturates, bismuth bromides cinchophen gold iodides mercury penicillin phenazone, phenytoin quinine salicylates sulphonamides
- Erythema nodosum iodides salicylates sulphonamides, thiouracil
- Exfoliative dermatitis arsenic (organic), barbiturates bismuth, gold, mepacrine, mercury phenolphthalein phenytoin streptomycin sulphonamides
- Fever arsenic barbiturates sulphonamides
- Genital lesions phenazone phenolphthalein, quinine
- Gingivitis bismuth mercury phenytoin (hypertrophy)
- Granulomatous, vegetating, ulcerative halogens
- Herpes simplex arsenic
- Infective (seborrhoeic) dermatitis arsenic gold, mepacrine mercury penicillin sulphonamides
- Keratoses carcinomata arsenic (inorganic)
- Leucopenia amidopyrine arsenic barbiturates phenazone sodium amino salicylate sulphonamides
- Lichenoid arsenic, bismuth, gold mepacrine
- Light sensitisation arsenic, gold mercury quinine sulphonamides
- Lupus erythematosus sulphonamides
- Papulo necrotic tuberculides calciferol
- Pigmentation arsenic barbiturates bismuth, corticotrophin gold mepacrine, phenazone phenolphthalein, quinine silver
- Pityriasis rosea like antihistamines arsenic, gold mepacrine
- Pruritus general codeine morphine opium also arsenic bismuth gold mepacrine penicillin phenobarbitone phenolphthalein Pyramidon, sulphonamides
- Pruritus anogenital chloramphenicol chlortetracycline codeine phenolphthalein

the flexural areas In the toxic forms the exfoliation develops uniformly during or after a course of treatment with one of the drugs mentioned In both these forms fissuring or secondary infection may develop and there may be considerable enlargement of the regional lymph nodes

In the idiopathic lymphadenopathic erythroderma the skin is dark brown and shiny and the exfoliative element less marked There is marked enlargement of the lymph nodes and those at the axillæ and groins may be observed bulging the skin In the male the breasts may become swollen and tender The patient may have other possibly toxic manifestations including psychosis cardiac irregularities etc There may be a moderate intermittent fever

In lymphoblastomatosis with erythroderma the skin is bright red and coarsely peeling The lymph nodes may be moderately enlarged and the liver and spleen palpably enlarged

In all forms of erythroderma heat loss is excessive and care must be taken not to expose the patient unduly during examination on the other hand occlusive ointments may interfere with heat loss and cause pyrexia There may be considerable loss of hair and thickening of the nails

Course and Prognosis —This depends on the cause The form due to over-treatment of a dermatosis slowly resolves with suitable bland treatment The toxic forms persist for some weeks or months depending on the rapidity of elimination of the toxic substance The severest examples may have a fatal outcome from broncho pneumonia hepatitis or nephritis The idiopathic form tends to clear after some months but may recur even after several years The lymphoblastic form is steadily progressive to a fatal ending

Diagnosis —The recognition of erythroderma is a simple matter and the diagnosis of the different forms has been indicated above But there are two conditions that can closely resemble erythroderma The first is psoriasis universale which can develop without any over treatment The history should help and the skin is bright red with mica like scales The nails may be abnormal in either condition but more particularly in psoriasis The blood count is normal in psoriasis but also in the earlier stages of lymphoblastic erythroderma The histology of both conditions is distinctive

The second condition which may be mistaken for erythroderma is pemphigus foliaceus (erythematodes) Here the pathological process of poor cell cohesion is so superficial (in the granular layer) that any bullæ that form are quickly broken and a picture of exfoliation and infection results Nikolsky s sign is positive and the histology characteristic the granular layer being exposed to the surface

In infants extensive staphylococcal pemphigus may have erythrodermatous characteristics (Ritter s disease)

Treatment —In all forms only bland applications should be used and they should not be occlusive Oily calamine lotion zinc cream or hydrous ointment are all useful Care should be taken that the patient does not get chilled by exposure

In the over treatment form this soothing treatment combined with such sedation as may be necessary is all that is required the patient being kept at rest in equable surroundings and the skin cleaned with a bland vegetable oil

In the toxic form dimercaprol is valuable where arsenic gold mercury or bismuth is believed to be responsible It is best given in a course of 6 days 2 ml 4 hourly on the first day 2 ml twice daily on the second third and fourth and 2 ml daily on the fifth and sixth days After this course daily intramuscular injections of 4 ml of crude liver extract may be given with advantage for a week followed by a second course of dimercaprol The patient should also receive vitamin supplements

In toxic erythroderma due to non metallic poisons the courses of dimercaprol are omitted but the intramuscular injections of crude liver extract may be given with benefit 4 ml daily

In the idiopathic form corticotrophin is invaluable for bringing about a remission

carbon dioxide snow applications and the carcinomata by X irradiation or carbon dioxide snow, depending on their size and situation. *Toxic effects from organic arsenic* need treatment with dimercaprol.

Rest in bed is advisable in the more severe eruptions. Plenty of fluids should be given. The urine should always be examined and treatment adjusted accordingly. *A blood count* is also advisable to detect hæmoglobin deficiency (as with dapsone) or leucopenia (as with sulphonamides, etc.). In purpuric eruptions the thrombocyte count should be estimated. If it is normal vitamin C should be given in large doses. If there is evidence of severe marrow depression, blood transfusions may tide the patient over the worst phase. In all forms of drug eruption multiple vitamin supplements are a rational treatment and crude liver injections are often helpful. Antihistamines are invaluable for controlling urticaria from penicillin, and once the optimum dosage has been found they are best given in gradually smaller doses until they can be abandoned. Local treatment is often unnecessary or may consist of the application of a lead and calamine lotion.

ERYTHRODERMA (EXFOLIATIVE DERMATITIS)

Erythroderma is a persistent redness of the skin, with exfoliation (as opposed to erythema, which is transitory).

Ætiology and Pathology.—There are numerous causes for this type of reaction. It may develop as a result of the over-treatment of eczema, dermatitis, infective dermatitis or psoriasis. It may be a toxic phenomenon following the administration of organic arsenicals, mercurials, sulphonamides, gold, barbiturates, bismuth or mepacrine. It also occurs in an idiopathic form as lymphadenopathic erythroderma, a condition which is probably toxic and sometimes recurrent, with much pigmentation (lipomelanic reticulosis).

Another form of erythroderma is associated with lymphoblastomatosis (*l'homme rouge*), sometimes preceding or following the clinical phenomenon of mycosis fungoides and ultimately being accompanied by an increase of circulating lymphocytes. An erythrodermatous form of sarcoidosis also occurs.

Histologically there is hyperkeratosis and parakeratosis, spongiosis with a variable degree of acanthosis and œdema, and an infiltrate of lymphocytes and histiocytes in the upper dermis and around the vessels and epidermal appendages. In the idiopathic form, there is much pigment in the melanophores of the dermis and the lymph nodes show little disorganisation but much melanin, hæmosiderin and lipoid material in the reticulum cells. In the lymphoblastomatous form there may be microabscesses in the prickle cell layer and either a basal infiltrate indistinguishable from the benign type already described or a massive infiltrate of lymphocytes or of lymphoblasts with eosinophils, neutrophils, histiocytes and reticulum cells, with many mitoses. This infiltrate is dense in the upper dermis and patchy in the deeper parts. The histological pattern of the lymph nodes is disorganised. It is sometimes difficult or impossible to differentiate, except by repeated sections at 3 to 6 months interval, between the relatively benign lipomelanic form and the malign reticulosis, but the clinical features are usually fairly distinctive, the former being characterised by much pigmentation and slight or moderate peeling, the latter by redness and marked peeling. The histology of the lymph nodes, the peripheral blood and bone marrow may all help to establish the diagnosis. Erythrodermatous sarcoidosis shows the histological features of sarcoidosis.

Clinical Picture.—In the over-treatment forms there is a history of a preceding more localised dermatosis and of its extension to the condition observed following the application of one or more known irritants or sensitisers. There is coarse peeling with moderate redness and sometimes a greasy texture to the scales, particularly in

Diagnosis—Guttate psoriasis has to be differentiated from a secondary papulo squamous syphilide on the basis of absence of lymph node enlargement or of mucosal involvement The skin lesions are not infiltrated or ham coloured in psoriasis and although the scalp may be affected there is no loss of hair

Infective (seborrhœic) dermatitis presents with dirty grey scales of greasy texture beginning as follicular papules which affect by preference the face sweat grooves and flexures the scalp is involved with loss of hair

In pityriasis rosea the lesions are pink or fawn coloured with a centripetal free border to the collarette and the malady usually affects the trunk and proximal parts of the limbs

Lichen planus presents with itchy violaceous polygonal papules with a waxy glance mostly on the flexor surfaces

Treatment—Calamine liniment makes the best local application All measures directed towards improving the general well being are likely to help including a holiday vitamin supplements and (if under skilled observation) ultra violet irradiation with a suberythema exposure daily

(2) Localized Extensor Psoriasis is another way in which the malady begins and it may persist with fluctuations for the remainder of the patient s life without any obvious disturbance in the general health This type may begin in childhood or in adult life and is most common at and just below the tip of the elbows and over the patella and patellar tendon Other sites often affected include the lumbo sacral region the calves the forearms and the scalp or any of these areas may be affected alone The lesions may be nummular discoid circinate polycyclic or irregular in shape (psoriasis geographica) There is usually no itching

Diagnosis—Nummular eczema may resemble a nummular psoriasis but the lesions are papulo vesicular exuding or crusted A single chronic patch of psoriasis has to be differentiated from lichen simplex lupus vulgaris tuberculoid leprosy tertiary syphilis Bowen s disease and superficial basal cell epithelioma (*q v*)

Treatment—The patient is best advised that treatment is only necessary for the sake of appearance and that the condition in no way interferes with general health and is not contagious At the same time a pessimistic view that psoriasis is incurable and nothing can be done about it is not only unjustified but positively harmful It is true that the fundamental cause of psoriasis is unknown and therefore cannot be removed nevertheless the precipitating factors causing recurrences and exacerbations are often discernible and it may be possible to adjust or remove them and so give relief to the skin condition The importance of day by day traumata in this form must be remembered particularly with regard to prognosis

In the localised form benefit is often derived from daily applications of a solution of coal tar to the lesions with a camel hair brush combined with soft paraffin ointment to any cracked or excessively dry areas as required Solution of coal tar may also be applied in a 6 to 12 per cent concentration with or without salicylic acid 2 to 4 per cent in ointment of wool alcohols simple ointment or soft paraffin ointment Ointment of wool alcohols mixes most with skin fats and so brings the tar into more intimate contact with the skin Simple ointment and to a greater extent soft paraffin ointment mitigate the action of the tar and they are often more useful because of their soft paraffin content

(3) Flexural Psoriasis is most commonly seen in the obese and friction between opposing surfaces of skin plays an important part The axillæ submammary folds umbilicus genito crural folds and intergluteal cleft may be affected Secondary infection may occur particularly with monilia Sometimes diabetes coexists Psoriasis of the genito crural region may be either the result or the cause of pruritus vulvæ The lesions are sharply marginated smooth shiny red areas

50 mg 8 hourly being given and the dose gradually reduced as improvement results The condition may remain clear after withdrawal of the drug or it may recur in which circumstances it is best to give cortisone in the smallest dose which gives relief and to withdraw it gradually as soon as possible

In the lymphoblastomatous form corticotrophin may give symptomatic relief without objective improvement beyond a slight diminution of scaling Radioactive phosphorus is worth a trial Otherwise treatment is symptomatic and supportive

SQUAMOUS DERMATOSES

PSORIASIS

Psoriasis is a common condition of sharply marginated, reddened areas of skin with abnormal scaling The malady is most variable in its intensity and course, remissions recurrences and exacerbations being a characteristic feature

Ætiology and Pathology —The fundamental cause is an unknown biochemical fault in epidermal cell formation resulting in abnormal horn cells The fault is inherited and psoriasis occurs in 1 in 5 on the average of children of a psoriatic parent The first signs are usually noted in the second or third decades but it may first appear in children under 10 or in persons over 30 or even in old age Histologically, there is parakeratosis (nucleated cells in the stratum corneum) some hyper keratosis and irregular acanthosis (hyperplasia of the stratum mucosum) with such gross variability in the thickness of the epidermis that at one site there may be only a few cells between the dermis and the surface while nearby there may be a large number There is clubbing of the interpapillary rete ridges of the epidermis In the dermis there is vascular dilatation particularly in the upper part and a patchy lymphocytic infiltrate around the vessels and the cutaneous appendages

Precipitating factors are the hereditary predisposition, infections unfavourable physical and emotional environments, emotional conflict and trauma to the skin

Clinical Picture —From the clinical standpoint, psoriasis is best divided into six types

(1) Guttate, post infective psoriasis of children
(2) Localised extensor psoriasis
(3) Flexural psoriasis
(4) Widespread psoriasis
(5) Pustular psoriasis of the palms and soles
(6) Psoriasis of the nails

(1) Guttate Psoriasis in Children may have no obvious precipitant but often there is a history of an infection particularly streptococcal throat infections some 3 weeks before the onset of the rash It may begin after scarlet fever or varicella measles or mumps suggesting that the malady is a type reaction of certain individuals to various infections

The lesions are raindrop sized pink, flat topped papules with scaling which is at first inconspicuous *Itching is slight or absent The scaling is made more obvious by scraping (grattage) a papule with a spatula (not a finger nail !)* This makes visible the silvery mica like delicate scales and pin point bleeding indicates the presence of dermal papillæ very near the surface The lesions are widespread even generalised in distribution but the face and hands tend to be less affected

Course and Prognosis —Provided the condition is not over-treated this form of psoriasis often gradually clears in about 3 months In others it may persist with enlargement of some of the lesions to coin like (nummular) or discoid areas *At any time in life there may be recurrences or recrudescences* of psoriasis usually of the discoid type the guttate form rarely returning

It is important in widespread psoriasis to do nothing that may cause an extension of the malady and possibly lead to its generalisation or to exfoliative dermatitis For this reason alone its more rigorous treatment needs daily supervision by a trained observer Dithranol has a justifiable reputation for relieving psoriasis but this treatment is best reserved for in patients Dithranol ointment (B P) (0 1 per cent) is in any case too weak to be of value while strong dithranol ointment (1 per cent) is too strong for out patient use and for the first trial of this substance Its injudicious use can cause aggravation or even exfoliative dermatitis It is best to start with 0 5 per cent *in soft paraffin and to raise this to 1 per cent 1 5 per cent or 2 per cent* in stages as may be required Dithranol causes an inflammatory reaction and stains the skin a violet brown colour Its daily application is continued until the lesions look paler than the surrounding skin It is then withheld and soft paraffin ointment is substituted Dithranol causes a severe conjunctivitis if it gets into the eyes

In resistant psoriasis T.A B injections are sometimes successful in intravenous doses of 25 50 and 100 million organisms at 5 to 7 day intervals the aim being on each occasion to attain a temperature peak of 103 F

Sedation with bromides promethazine hydrochloride or barbiturates may be necessary and depressed patients may do well on amphetamine sulphate 5 mg each morning Dietetic and vitamin treatment is ineffective except in so far as conditions of obesity on the one hand or malnutrition on the other may require adjustment X ray irradiation (100 r three times at weekly intervals) is very effective in clearing individual patches but is only justifiable for special purposes such as the clearance of a resistant patch on a site for operation

Psoriasis does not respond to corticotrophin or cortisone

Emotional factors may be dealt with according to their relative importance by reassurance open discussion and moral support by drug abreaction or even by psychoanalysis Suggestion and hypnosis are undoubtedly helpful while they are used but are likely to cause an excessive rebound when the moral prop is withdrawn

Complete clearance of all lesions is the aim but the physician may well decide to be satisfied with some 80 to 90 per cent of clearance particularly if the psoriasis has appeared early in life and has been aggravated by relatively trivial stimuli At this stage the patient should be encouraged to live with the psoriasis and not to be forever trying to clear off the last traces by any new method recommended by all and sundry It must be stressed that the treatment of psoriasis is the treatment of each individual according to the physical or psychical defects that are discovered it is not a routine matter of one regime or another

A holiday in congenial surroundings with relaxation and isolation from the telephone may be as effective as any of the above measures

(5) Psoriasis of the Palms and Soles —This condition is probably identical with pustular bacteride and one form of acrodermatitis pustulosa continua

Clinical Picture —In pustular psoriasis the lesions are golden yellow from the beginning and do not go through a vesicular stage The pustules occur on palms or soles less often on fingers or toes amongst areas of red skin with dyskeratotic scaling Psoriasis may also occur on the palms as patchy dyskeratotic areas with some adjoining erythema On grattage silvery scaling is apparent Either form may occur with or without psoriatic lesions elsewhere

Course and Prognosis —Pustular psoriasis is extremely chronic and often fails to respond to remedies that are effective elsewhere including X rays Its relief depends on the discovery and treatment of any infective focus (particularly streptococcal) the avoidance of local physical traumata and treatment of any metabolic or emotional factors that seem to be relevant

Diagnosis is from pompholyx in which the vesicles are skin coloured and become yellow at a later stage

Diagnosis —The presence of psoriasis elsewhere usually helps in differentiation from infective dermatitis and from intertrigo

Treatment depends on the cause Obesity, diabetes various causes of pruritus vulvæ (*q v*) need attention Locally, magenta paint can be used to control any infective element After this, a dusting powder may be helpful or simple ointment with a 2 per cent solution of coal tar A 2 per cent salicylic acid and sulphur ointment may prove useful

(4) WIDESPREAD PSORIASIS may develop *de novo* or it may follow guttate psoriasis or localised psoriasis of the extensor or flexor surfaces The reason for the extension may be some infection over treatment, intoxication, bad environmental conditions or emotional stress due either to environmental or to personal difficulties There may be no constitutional disturbance but mental depression is common A persistent widespread rash may easily induce the leper complex and this accounts for the depression in some cases but in others the variation of mood is parallel with changes in the state of the skin neither preceding nor following them and suggests that fluctuations in intensity of the psoriasis and mood changes are often due to a common cause The involvement may be widespread, subtotal or universal The lesions may be nummular, discoid figurate polycyclic or annular The Koebner phenomenon may be present in which scratching the skin causes the development of psoriasis in the line of scratch The skin in the centre of annular lesions does not show this reaction having become refractory for a time to this stimulus The sites commonly affected include the scalp (where the scales may be in several diminishing layers giving a limpet like appearance—rupioid psoriasis), the trunk, particularly the lumbo sacral region the extensor surfaces of the limbs and the nails Sometimes the flexures are also affected The face and hands usually escape except in severe examples of the disease Arthritis of the rheumatoid type is commonly associated with extensive psoriasis

Course and Prognosis —This severe form of psoriasis is of prolonged duration and uncertain often unfavourable prognosis unless the causal factors can be controlled

Treatment —It is advisable to admit patients with extensive psoriasis to hospital for investigation and treatment The investigations are directed to infective metabolic and emotional disorders and specific treatment is given accordingly Nonspecific treatment for the psoriasis is best carried out by the Goeckerman régime or some modification of it In this the patient s skin is cleaned of ointment with liquid paraffin each morning then general ultra violet irradiation is given a first degree exposure with treatment of plaques of psoriasis with a second degree exposure if this is practicable The patient next takes a warm bath (to which may be added 2 to 4 oz of solution of coal tar to 25 gallons of water if itching is severe) In the bath the whole surface may be cleaned with a toilet soap but forcible removal of scales with a coarse brush is inadvisable After drying from the bath the patient is treated by the inunction of 6 per cent solution of coal tar in soft paraffin, excepting the flexural lesions which are better dealt with more gently with Lassar s paste alone or with 2 per cent of the solution of coal tar The scalp needs special attention Equal parts of Teepol and water with 1 per cent of glycerin make an effective shampoo, followed by the inunction of up to 12½ per cent of solution of coal tar in the ointment of wool alcohols or in emulsifying ointment To this may be added 2 per cent of salicylic acid and 2 5 per cent of ammoniated mercury (Soft paraffin is too sticky and messy in areas of coarse hair and Lassar s paste causes matting and is very difficult to remove) Oil of cade 12½ per cent may be used instead of the solution of coal tar or 2 per cent each of salicylic acid and of sublimated sulphur may be preferred in emulsifying ointment The régime may include autohæmotherapy 10 ml on four occasions every 5 days

the herald patch distribution of the eruption cleavage line tendency and centripetal scaling are characteristic Lichen planus is usually very itchy the lesions give a waxy glance , show pseudoscaling have a characteristic distribution and often involve the oral mucosa and the external genitalia

Course and Prognosis—If untreated the condition may persist indefinitely but it seems to have no effect on the general health

Treatment—The malady sometimes responds well to general ultra violet irradiation or to calciferol by mouth in a dose of up to 150 000 units a day for up to 3 months with fortnightly urine examinations and estimations of the blood urea to detect early signs of intoxication from the drug

Locally salicylic acid ointment is suitable

PARAPSORIASIS DISCOIDES (parapsoriasis en plaque xanthoerythroderma perstans) presents as yellowish red discs and ovals non itchy occurring on the trunk and limbs usually in adults aged 30 or more without constitutional disturbance

Histopathology is not distinctive There is focal parakeratosis and spongiosis and nonspecific infiltrate in the dermis a picture resembling a low grade dermatitis

Clinical Picture—Non itchy brown pink plaques appear on the trunk and the limbs with slight scaling and with no constitutional disturbance There may be slight atrophy

Course and Prognosis are both uncertain Parapsoriasis en plaque may persist for months or years and a proportion of the cases pass on to poikiloderma (telangiectasia atrophy pigmentation and depigmentation) or to reticulosis in one of its many guises (exfoliative dermatitis mycosis fungoides etc) The prognosis must be non committal and periodic physical examinations and if necessary biopsies should be made for early evidence of a reticulosis

Treatment is most unsatisfactory the malady resisting all efforts of the physician including ultra violet irradiation calciferol and various nonspecific remedies

PARAPSORIASIS LICHENOIDES (parakeratosis variegata) presents with reddish brown scaly flat topped papules in reticular pattern chiefly on the extensor surfaces of the limbs the neck and the trunk The condition is slowly progressive but benign

Diagnosis is from secondary syphilis and lichen planus (*q v*)

Treatment is symptomatic and supportive

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA is a fourth and uncommon form of parapsoriasis of more sudden exanthematous onset with lichenoid and varioliform lesions yellowish brown and crusting It resolves spontaneously after weeks or months leaving depressed scars The palms soles and mucosæ escape but the lymph nodes may be enlarged

Diagnosis is from varicella secondary syphilis drug eruptions pityriasis rosea and lichen planus (*q v*)

Treatment is symptomatic and supportive

PITYRIASIS ROSEA

PITYRIASIS ROSEA is a scaly disease of limited duration characterised by the appearance of a herald patch a few days before a generalised eruption

Ætiology and Pathology—The cause is unknown It often follows an upper respiratory infection or slight fever and may be a virde Second attacks are rare

The histopathology is not distinctive There is some parakeratosis and a non specific cellular infiltrate in the dermis

Clinical Picture—Children and young adults are mostly affected There is often a history of malaise coryza and of sore throat a week or two before the onset

Treatment —Locally, soft paraffin ointment with 2 per cent. salicylic acid is a useful application Tonsillectomy has been followed by relief in some cases X rays in fractional (100 r) exposures up to four may help, but as often fail

(6) Psoriasis of the Nails usually occurs with psoriasis elsewhere but occasionally it is the only evidence of the disease

Clinical Picture —The mildest form is a thimble like pitting of the nail plates This may vary in extent from a single pit on one nail to confluent affection of several nails and is very characteristic of psoriasis rarely being seen in other diseases affecting the nails

In the next degree of severity psoriasis causes brown or yellow discolouration affecting the sides or the distal parts or the whole surface of the nail plates In this form the nails are usually not thickened but when psoriasis affects the nail beds and matrices, the nail plates become thickened opaque, dull and friable Paronychial involvement causes deformity with longitudinal or transverse ridging and grooving

Diagnosis —Psoriasis unguium has to be differentiated from tinea unguium and eczema dermatitis affecting the nail folds Rarer possibilities include syphilis lichen planus and idiopathic nail dystrophies

Ringworm usually affects one or a few nails of the hands and feet in asymmetrical fashion and is often associated with ringworm elsewhere in toe clefts on the feet or hands or in the groins Microscopic examination of nail shavings removed with the edge of a glass microscope slide reveals fragments of mycelium The nails in ringworm are usually a dirty grey colour partly destroyed and deformed with longitudinal or transverse ridging and a powdery friable surface

Syphilis or lichen planus are recognised by evidence of the presence of these maladies elsewhere Idiopathic nail dystrophy is a discoloured and deformed condition of the nails without evidence of psoriasis or of other skin disease elsewhere

Treatment —In the minor forms treatment is not necessary unless the patient demands it The results of treatment are always uncertain but weekly applications of thorium-X 1500 e s u per ml for about 3 months often seem to give good results This treatment is preferable to the use of X-rays or medication with liquor arsenicalis Salicylic acid ointment makes a satisfactory local application Trauma to the nail folds and excessive drying or degreasing must be avoided

PARAPSORIASIS

Parapsoriasis is a descriptive term for various forms of persistently abnormal scaling of the skin They are rare and of unknown cause but are probably distinct conditions

Parapsoriasis Guttata (pityriasis lichenoides chronica) occurs as guttate grey brown scaly lesions the scales often being concave and not having the mica like appearance and pinhead bleeding points of psoriasis They are distributed on the trunk and limbs The lesions itch little if at all and there is very little redness of the skin around the abnormal scaling The lesions persist, with slight fluctuations for an indefinite period and there is no constitutional disturbance It usually affects young or middle aged adults

Pathology —There is parakeratosis and hyperkeratosis slight atrophy of the stratum mucosum and a nonspecific infiltrate of slight degree around the vessels and appendages in the dermis

Diagnosis is from secondary syphilis lichen planus drug eruptions and pityriasis rosea After a time the prolonged course rules out syphilis and pityriasis rosea In syphilis mucosal changes condylomata enlarged lymph nodes and evidence of a primary lesion may be found and the lesions are ham coloured In pityriasis rosea

brittle The plaques are pink or red scaly areas having a resemblance to psoriasis on the one hand and lichen simplex on the other, but they differ from both these conditions in that central circles or polycyclic areas of normal skin are present Ectropion may occur The mucous membranes are not affected There is no obvious constitutional disturbance

Course and Prognosis —The malady comes on insidiously and continues indefinitely in spite of treatment A spontaneous remission may occur after several months

Treatment —There is no evidence that the administration of vitamin A shortens the duration Œstrogens may seem to bring about a remission but their evaluation is difficult Treatment is symptomatic with applications of salicylic acid ointment or a mixture of this with an equal part of glycerin of starch

DYSKERATOSIS FOLLICULARIS

Dyskeratosis follicularis or Darier s disease is a rare condition due to an inherited abnormality of horn formation

Ætiology and Pathology —The cause is unknown but an abnormality of vitamin A metabolism is suspected

The highly characteristic histology consists of hyperkeratosis and papillomatosis with keratotic plugging and dyskeratotic corps ronds and grains in the upper epidermis with lacunæ at the epidermo dermal junction which results in the formation of vegetations

Clinical Picture —Early in life the child is noted to have dirty grey keratotic plugs on the skin The flexures and the hair bearing areas are affected most Secondary infection may lead to moist warty nodulation and an offensive odour The finger tips show pinhead and smaller depressions on the epidermal ridges They are peculiar to this malady

Course and Prognosis —The course is prolonged but the malady does not disturb the general health except from the effects of secondary infection Some degree of mental retardation is not uncommon

Diagnosis is from acanthosis nigricans in which there are velvety pigmented folds and wartiness and from pemphigus vegetans and dermatitis vegetans (*q v*)

Treatment is symptomatic Ten per cent salicylic acid ointment is a useful application Vitamin A is ineffective

LICHENOID DERMATOSES

These eruptions are of widely differing ætiology and pathology but they have in common some degree of similarity in their physical signs

LICHEN SIMPLEX CHRONICUS

This is a common condition in which oval areas of pinkish brown thickened skin develop at sites of repeated friction (see Sensory Disorders)

LICHEN PLANUS

This is a disorder of uncertain duration in which itchy flat topped shiny violaceous papules appear on various parts of the body

Ætiology and Pathology —The cause is unknown It is suspected to be of virus origin and set off by varied noxæ including drugs physical agents nutritional deficiencies and emotional stresses

Histologically the picture is characteristic but it is modified by the amount of

The *first change* in the skin is the herald patch, somewhere on the trunk at the axilla or on a thigh, occasionally *more distally on a limb*. The lesion is an oval, rosy plaque becoming fawn coloured with scaling, the free edges of the scales being centripetal. Itching is *slight or absent as a rule*. The herald patch may be missed. The generalised eruption begins *a week or two later* and is usually confined to the trunk and proximal parts of the limbs. It often extends up the neck and down the arms and *forearms*, but the face, lower thighs and legs are seldom affected.

Two types of *generalised* eruption are seen: the more usual macular and plaque form and the follicular *papular form*, in which, however, a few plaques are always present as well. The plaques start as pink macules which extend to become oval '*medallions*' which, on the trunk, lie parallel to the ribs; they vary in size from *0.5 cm. to 2 cm. or more*. Scaling is not apparent at first but, after a week or 10 days, the lesions become fawn coloured and scaling begins from their centres causing a *centripetal* arrangement of the free border of the scaling. In the early stage when *this feature* is not apparent, it can be demonstrated by scraping a lesion so as to detach the looser scales. There are no mucosal changes and the lymph nodes are not enlarged.

The follicular papular variety is more difficult to recognise, but the manner of *onset and* the distribution should give rise to suspicion and the discovery of medallions makes the diagnosis clear.

Course and Prognosis.—The total course is usually about 6 weeks but it may *last only* 4 weeks or continue for anything up to 10 weeks. Pityriasis rosea is modified in xerodermatous and seborrhœic subjects. Its course is prolonged if, owing to a misdiagnosis, treatment is given with fungicides. In these circumstances, it may become papular vesicular, eczematised and distressingly itchy.

Diagnosis is from secondary syphilis, drug eruptions, tinea circinata and infective dermatitis. In secondary syphilis, the examination of the genitalia, mucous surfaces and lymph nodes reveals other evidence of that disease. Pityriasis rosea-like drug eruptions are usually in some way atypical. Tinea circinata is usually more acute with vesiculation as well as marginal peeling; the lesions are circular rather than oval; they are few in number and may appear on the face; the scalp too may be affected with scaling and short broken hairs. Microscopy reveals mycelia and *spores*. Infective dermatitis is recognised by its grey greasy scales and sweat area distribution.

Treatment.—Reassurance, explanation and calamine lotion are usually all that are required. The patient need not be isolated. Warm but not hot baths may be taken. If any doubt exists, the Wassermann reaction should be tested. Over-treatment must be avoided. To hasten peeling, general ultra-violet irradiation is sometimes given and the course may be shortened by about a week in this way, but there is rarely any justification for this procedure.

PITYRIASIS RUBRA PILARIS

This is a rare chronic skin disorder characterised by red follicular papules with horny spines, keratoderma of the palms and soles and psoriasis-like plaques of a bright pink colour.

Ætiology and Pathology.—The cause is unknown. A defect of vitamin A metabolism is suspected. It may be a follicular variant of psoriasis.

Histologically there is follicular keratosis and plugging with an infiltrate around. The psoriasis-like plaques show parakeratosis and a nonspecific infiltrate.

Clinical Picture.—There are widespread groups of pink or red follicular papules with keratotic tips on the body and limbs. The hairy backs of the proximal phalanges show follicular keratoses. There is marked thickening and dirty discolouration with fissuring of the horn on the palms and soles and the nails become deformed and

lichen nitidus lichen sclerosus et atrophicus and lichen amyloidosis (q v) The diagnosis depends on a careful consideration of the elementary lesions their waxy glance' their distribution and the presence of orogenital lesions Lichen planus may be non itchy and in the early stage of evolution the lesions may be atypical Hence it is sometimes necessary to reinspect a patient after a week s interval with a view to coming to a firm diagnosis It may also be necessary to perform biopsy a very useful procedure because of the highly characteristic histology in lichen planus

Treatment —There is no specific treatment for lichen planus and each patient must be dealt with according to the relative significance of emotional drug physical or other factors that become evident when taking the history

Sedation is usually necessary either by an evening dose of a barbiturate such as butobarbitone gr 3 or with gr ¼ doses of phenobarbitone two or three times a day in addition

The withdrawal of any drugs the patient may have been taking is advisable if they are suspected as causal for example gold or mepacrine Appropriate detoxicating remedies such as dimercaprol should be given when indicated and more specific supporting treatments such as crude liver injections and vitamin supplements are justifiable

Bed rest is a valuable prescription for subacute widespread lichen planus or when the history suggests that fatigue may be an important factor Such adjustments to the patient s mode of living that may seem necessary play an important part in treatment and unless these psycho physical factors are dealt with the malady may prove intractable

Certain drugs have a reputation for relieving resistant lichen planus They include mercury and potassium iodide mixture intramuscular injections of bismuth (0 2 g in 1 ml) or of mercury salicylic arsonate (0 06 g in 2 ml) or a short course of Fowler s solution A short course of corticotrophin may bring about a remission

Fractional X ray exposures (75 r up to four weekly treatments) to confluent patches or fortnightly applications of thorium X (1 500 e s u per ml) often help to tilt the balance in the patient s favour

Other local applications are not of great value Phenol 1 per cent in zinc cream or calamine lotion may be used as an antipruritic

LICHEN NITIDUS

This is a rare eruption of uncertain ætiology consisting of lichenoid papules in which there are focal areas of tuberculoid histology enclosed as it were between claws of epithelium The overlying epidermis is atrophic The collagen and elastin are degenerate A tuberculous cause has not been established and the condition may in fact be a variant of lichen planus

Clinical Picture —Non itchy skin coloured or pink shiny flat topped papules occur in close set groups particularly on the penis the flexor surfaces of the forearms or on the abdomen

Course and Prognosis —The lesions persist indefinitely but may finally fade away without residual pigmentation

Diagnosis is made from lichen planus by the absence of itching and pigmentation and the characteristic histology

Treatment is ineffective Success has been claimed for iodine taken by mouth in the form of Lugol s solution The patient should be examined for any possible tuberculous focus

LICHEN SCLEROSUS ET ATROPHICUS

A condition of lichenoid papules ending in atrophy and sclerosis affecting both sexes commoner after 30 years of age rare in children

atrophy or hypertrophy present and by the extent of involvement of hair follicles. Hence, terms such as lichen planus atrophicus lichen planus hypertrophicus (lichen planus verrucosus) and lichen plano pilaris (lichen planus follicularis) Lichen spinulosus et folliculitis decalvans of Graham Little is a variety of lichen plano pilaris affecting the scalp

There is hyperkeratosis, thickening of the stratum granulosum, either atrophy of the stratum mucosum or an irregular acanthosis and, depending on the intensity of the dermal infiltrate a variable degree of liquefactive degeneration of the stratum germinativum which in extreme cases may result in histological or even clinical evidence of bulla formation (lichen planus bullosus) The rete ridges may be of saw tooth' type or in atrophic areas absent in hypertrophic cases there is papillomatosis In the upper dermis, immediately subjacent to the epidermis, is a heavy infiltrate almost entirely composed of lymphocytes with a few histiocytes

In lichen plano pilaris the same histological features are observed at and around the hair follicles

Clinical Picture—Lichen planus most characteristically affects the buccal mucosæ the fronts of the wrists the lumbosacral region, the external genitalia the medial aspects of the thighs, the shins, calves and ankles it may appear on the palms or soles and anywhere on the body though rarely, if ever, on the face Scratching sometimes causes linear lesions (Koebner s phenomenon) or exposure to sunlight may localise the rash Involvement of the scalp with lichen plano pilaris may end in the picture of pseudopelade (*q v*) and rarely the nail matrices are affected and the nails dystrophic and deformed as a result

The elementary lesion of lichen planus as seen on the skin is a violaceous, polygonal flat topped shiny papule Sometimes the papules are only a shade darker than the surrounding skin Often Wickham s striæ and spots can be seen upon them—grey streaks and spots of pseudo scaling thought to be colour changes caused by the thickened stratum granulosum The individual papules often enlarge or run together to form extensive plaques

Central healing, often somewhat atrophic is common, resulting in lichen planus annulare On the penis this is most characteristic and the lesions here are often non itchy Resolution of lichen planus is nearly always accompanied by a great deal of pigmentation It is not unusual for all the lesions to clear except those on the legs which may on the contrary, become verrucose and persist indefinitely

Lichen plano pilaris presents as shiny follicular papules with a violaceous rim the papules often being grouped The process ends in atrophic scarring at first violaceous later white and in patchy baldness

Lichen planus of the mouth gives rise to white slightly raised polygonal spots and white streaks and delicate feathery patterns Ulceration or redness are unusual and the lesions are either symptomless or give rise to a sensation of slight roughness

Lichen planus of the nails is very rare Involvement of the nail matrices may cause grey rough dystrophic nails

Course and Prognosis—Lichen planus is extremely variable and unpredictable in its course, no doubt depending on the possibilities of controlling the causal factors The subacute form may in fact persist for months new lesions appearing while others become inactive and are concerted into pigmented macular remnants The chronic form may persist indefinitely or clear at some sites but not at others The legs are particularly likely to be affected by chronic and often hypertrophic lichen planus Even after complete disappearance of all lesions fresh outbreaks may occur some months or years later

The development of carcinoma on lichen planus in the mouth has been described in a very few cases lesions on the vulva because of the irritation they cause may result in leucoplakic changes and carcinoma

Diagnosis is from psoriasis parapsoriasis guttata syphilis, warts lichen simplex,

(phrynoderma) The cause is believed to be a deficiency of vitamins A and C and the malady is mostly seen in children

A somewhat similar picture may occur in the follicular variety of xeroderma (keratosis suprafollicularis)

An eruption of oval areas of lichen spinulosus on the trunk and limbs may occur with fungous infections of the feet (lichen trichophytide)

Pathology—In xeroderma the stratum granulosum is deficient In avitaminosis A and C there may be perifollicular hæmorrhages

Diagnosis is from lichen plano pilaris in which the papules have violaceous rims and on the scalp cause a variety of folliculitis decalvans

Treatment—Depending on the cause treatment consists of vitamin supple ments elimination of a fungous infection or attention to xeroderma or lichen planus Salicylic acid ointment may be applied

LICHEN SCROFULOSORUM

This is an eruption of skin coloured or pink lichenoid papules usually occurring on the trunk in childhood There is often also tuberculosis of lymph nodes bones or joints etc a strongly positive Mantoux reaction and a tuberculoid histology (see Tuberculides)

LICHEN AMYLOIDOSIS

This is a localised cutaneous form of amyloidosis presenting as itchy elevated nodular plaques on the shins resembling hypertrophic lichen planus The diagnosis is confirmed by staining for amyloid (see Amyloidosis)

LICHEN URTICATUS

This is a papular urticaria of childhood The lesions resemble varicella more than lichen (see Urticaria)

PITYRIASIS LICHENOIDES CHRONICA

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA

(See Parapsoriasis)

PARAPSORIASIS LICHENOIDES

(See Parapsoriasis)

LICHENOID ERUPTION OF AXILLÆ (FOX FORDYCE DISEASE)

This malady occurs mostly in women as pink or brown dome shaped grouped papules in the axillæ also sometimes at other apocrine sites the areolæ of the nipples the umbilicus pubic region and the perineum Itching is severe

Ætiology and Pathology—The cause is unknown

There is follicular hyperkeratosis and plugging acanthosis and a chronic inflam matory infiltrate around the apocrine glands

Treatment consists of œstrogens by mouth and salicylic acid 2 per cent in hydrous ointment locally Fractional X ray exposures 100 to 150 r weekly up to a total of 600 r may prove helpful

ACNEIFORM DERMATOSES

These are eruptions in which acuminate papules provide the most characteristic feature

Ætiology and Pathology—The ætiology is unknown

The histopathology is characteristic and includes hyperkeratosis and acneiform follicular keratotic plugging atrophy of the stratum mucosum, œdema of the upper dermis with homogenisation of the collagen and an inflammatory infiltrate in the deeper parts of the dermis, without obliterative vascular changes as seen in scleroderma

Clinical Picture—The malady presents with genital and extragenital lesions In both sexes the latter consist of roughly circular pinkish grey atrophic parchment like patches with a few comedones At flexural sites there may also be white lichenoid papules and scleroderma like plaques without comedones

In the male the genital lesions may be similar to those already described if they are on the shaft of the penis There may be a fibrous constriction of the prepuce causing phimosis On the inner surface of the prepuce, at the coronal sulcus and on the corona and glans there is a variable degree of atrophy and sclerosis Atrophy may be confined to the penile meatus and this may later cause some urethral stenosis or the whole surface of the glans may be irregularly thickened dry white and hard a condition known as balanitis xerotica obliterans In the female the atrophic and sclerotic changes may affect the labia minora or majora and the adjoining skin of the perineum and perianal region Itching is variable but may be intense The severest cases may have bullous lesions owing to interference with lymph drainage

Course and Prognosis—Lichen sclerosus et atrophicus continues indefinitely but may undergo considerable spontaneous improvement There are no serious complications on the extragenital skin but on the penis urethral stenosis may occur and on the vulva intense itching and scratching may lead to leucoplakic and carcinomatous changes

Diagnosis is from the localised form of scleroderma (morphœa) macular atrophy, leucoplakia and atrophic vaginitis with kraurosis

Morphœa presents as an oval firm white or pink, shiny plaque with a lilac halo Atrophy is not marked except sometimes in the later stages There are no comedones The histology is different from that of lichen sclerosus et atrophicus In macular atrophy there are soft bulgings giving a hernia like feeling on pressure Leucoplakia only affects mucous surfaces Lichen sclerosus et atrophicus of the vulva may be complicated by leucoplakia Atrophic vaginitis presents as shrinkage of the vaginal orifice (kraurosis vulvæ) with patchy pigmentation depigmentation atrophy and telangiectasia of the mucosa of the vulva The labia minora are often atrophic or absent

Treatment—There is no specific treatment It has been claimed that vitamin E by mouth is of value The ointment of wool alcohols or hydrous ointment make useful local applications Meatal stenosis may need suitable attention If leucoplakia or carcinoma supervene on the vulva excision is called for, but excision of the perineal and perianal skin is unnecessary because carcinoma does not develop on extragenital lesions of lichen sclerosus

LICHEN STRIATUS

This is a rare malady occurring usually in children A band of lichenoid papules erupts usually in the long axis of a limb and after a few weeks or months involutes spontaneously Itching is slight or absent

The histology is that of chronic dermatitis

Diagnosis is from lichen planus linearis

Treatment is symptomatic and supportive

LICHEN SPINULOSUS (KERATOSIS FOLLICULARIS)

This is a condition of widespread or grouped horny follicular papules The widespread form involves in particular the extensor surfaces of the limbs and trunk

Diagnosis is from sycosis acneiform tuberculides syphilides drug eruptions and rosacea

In sycosis involvement is of coarse hair bearing areas whereas acne involves areas of glabrous skin and the borderline between coarse hair bearing areas and glabrous skin The two conditions may coexist

Acne agminata presents as grouped translucent papules particularly on the eye lids nose and penis

Acneiform syphilides are papulo pustular but without comedones, but syphilis may also aggravate a pre existing acne vulgaris

Halogens too particularly iodides may cause acneiform eruptions without comedones or aggravate pre existing acne vulgaris *Halogen acne is usually more exuberant than acne vulgaris* Occupational acne often affects the forearms and thighs as much as the face

Rosacea usually occurs in an older age group than acne vulgaris but occasionally starts in the teens *The lesions involve an oval area of the centre of the face* They are erythemato papular and pustular but there are no comedones though scars of *previous acne may remain* There is *marked vasolability and the face is bright red* not the muddy colour of acne vulgaris

Treatment depends on control of the primary cause and of the aggravating factors The primary cause is a relative excess of *androgens in relation to œstrogens* The aggravating factors are numerous They include a familial predisposition dietetic errors certain drugs contact irritants imperfect hygiene and insufficient weathering and emotional tension related in particular to conflicts with parental authority and difficulty in psychosexual adjustment to adult life the acne sufferer often being somewhat retarded in this respect while intellectually adequate and physically mature

Treatment aims at correcting the endocrine imbalance so as to diminish sebaceous over activity and attaining and retaining patency of the pilosebaceous follicles

It is inadvisable to use œstrogens in the male in the dosage necessary to give a good result the emasculating effects that also result are undesirable Emotional changes and gynæcomastia may result In females œstrogens may justifiably be given if there is oligomenorrhœa irregular menstruation male type hirsutism or marked aggravation of the acne before the menses but it is inadvisable to use them even in these circumstances for the first few years after the menarche it is better to allow time for menstruation to acquire a regular rhythm

When prescribing œstrogens for acne the patient should be asked to estimate the expected first day of the next menstrual period and to begin the treatment 10 days *before this date and continue until menstruation begins In this way there is no* interference with ovulation If menstruation is markedly irregular it is not possible to adopt this *procedure* and the patient *is instructed to start treatment a fortnight* after the last day of the previous menstrual flow and continue for a fortnight or until the next period begins whichever is the shorter This treatment is continued for 3 to 6 months

The diet should be high in protein and vitamin content Excess of fats and carbohydrates must be avoided In particular chocolate cocoa cream pastries and cheeses are liable to aggravate acne

Bromides and iodides have in the past been responsible for much aggravation of acne but they are in less common use to day Other drugs for example aspirin occasionally aggravate acne

The skin should be washed at least twice a day with a good toilet soap Medicated soaps are best avoided If cosmetics are used they should be of the lotion type not creams The patient should be discouraged from experimenting with local applications Irritant or sensitising substances incorporated in a base capable of mixing well with fat and water may cause a severe chemical folliculitis Similarly exposure

ACNE VULGARIS

A papular condition due to hyperkeratotic plugging of the pilosebaceous follicles combined with hyperplasia of the sebaceous glands

Ætiology and Pathology—Acne is brought about by an imbalance between androgenic and œstrogenic hormones In the male, an excess of testosterone is responsible, in the female, an excess of progesterone is believed to be the cause In either case there is a resultant sebaceous hyperplasia and a diffuse hyperkeratosis which at the pilosebaceous orifices particularly at the openings of glabrous hairs causes obstruction to the flow of sebum A blackhead (comedo) is an hyperkeratotic follicular plug This follicular obstruction leads to inflammatory changes (papular acne) the keratin and sebum having a foreign body effect This inflammation may end in resolution or in suppuration (pustular acne) in either case the end result is some degree of fibrosis The pus is usually sterile and if the suppuration is deep it may form cystic swellings in the hypoderm (acne conglobata) Burrowing tracks may form lined with epidermis and there may be small epidermal bridges and tunnels with several openings

Severe acne tends to end in keloid formation, particularly at the nucha over the sternum and, with smaller lesions on the face and neck (acne keloid)

In addition to the cystic swellings already mentioned, epidermal cysts of pinhead size may be interspersed amongst the acne lesions (' white ' acne)

There is no evidence that the acne bacillus is the cause of acne This organism is, like the pityrosporon of Malassez and the *Staphylococcus saprophyticus*, a secondary invader of the truly seborrhœic skin Some comedones contain an acarus, the demodex folliculorum Most acne lesions are sterile but sometimes there is a heavy secondary infection with staphylococci (acne sycosis) in these circumstances the pustules are notably more superficial and contain liquid pus as opposed to the cheesy contents of many acne pustules

Clinical Picture—Slight degrees of acne at puberty are so common as to be regarded as physiological It usually begins at about 12 to 14 years of age and diminishes in severity at 18 to 20 In girls it often coincides with the menarche Occasionally acne persists into adult life and may even last throughout life As a rule, males are more severely affected than females

Acne affects the face and neck, the upper trunk and to a lesser degree the lumbar region buttocks and limbs

A comedo (blackhead) (acne punctata) is a black or dirty grey pinhead sized hard speck at a pilosebaceous orifice In an uncomplicated comedo there is no redness or swelling but when this occurs an acne papule results acuminate firm and comedo topped liquefactive changes lead to a deep seated pustule This may resorb or break spontaneously or be broken by the patient s manipulations, and a funnel like, depressed scar results Lesions of acne conglobata are obtuse, dome shaped bluish-grey nodules It is not unusual to see comedones papules pustules small epidermal cysts cystic swellings and scars, often keloidal in the same patient

The complexion in acne is greasy and muddy, the thickened epidermis diminishing transmission of colour from blood flowing in the superficial vessels of the dermis Visibly enlarged patulous follicles are present and excessive sebum formation may be visible especially at the alæ nasi There may be an increase of dandruff but this is by no means the rule The acne patient of either sex is usually somewhat hirsute and in females the pubic hair often has a masculine distribution There may also be hyperidrosis

Course and Prognosis—Acne vulgaris usually clears up or improves considerably after the teens If it does not some cause can usually be found (see below) A variable amount of scarring is inevitable except in the milder forms

the first few days after birth It has been suggested that these are due to androgenic hormonal influences (progesterone) from the mother

(2) The use of camphorated oil olive oil or tallow as an embrocation may cause an acneiform eruption on the face or chest (grouped comedones)

(3) Excessive and occlusive wrapping up of the child s body may by increasing sweating on the face cause some inflamed follicular papules

(4) Occasionally cod liver oil given by mouth causes acneiform papules

(5) Unilateral nævi consisting of grouped comedones occur

(6) Adrenocortical neoplasms are accompanied by acne as is the administration of corticotrophin or cortisone

ROSACEA (ACNE ROSACEA) (see p 1207)

ACNE NECROTICA (ACNE VARIOLIFORMIS)

This is a relatively rare inflammatory condition of the follicles with discrete papulo pustulation on the forehead scalp and temples going on to necrosis and scarring

Ætiology and Pathology—The condition is a folliculitis due to coagulase-positive staphylococci Histological changes of acne vulgaris are present with the addition of œdema and an inflammatory infiltrate leading to superficial follicular necrosis

Clinical Picture—The patients are usually middle aged men but women may also be affected Near the hair margin across the forehead at the temples and on the neck are discrete brownish papules pustules and scabs with depressed scars It may also appear on the face limbs and trunk There may be much itching and picking of the lesions which are present in all stages at the same time Affected individuals usually show evidence of the seborrhœic state

Course and Prognosis—The condition tends to persist indefinitely and to relapse after treatment is stopped

Diagnosis is from seborrhœic folliculitis acne vulgaris syphilis and variola The duration distribution itching and polymorphic lesions suggest the correct diagnosis Seborrhœic folliculitis leaves little or no scarring

Treatment which is usually effective consists of the application of the appropriate antibiotic depending on sensitivity tests The associated seborrhœic state must receive attention Other remedies sometimes used include zinc and copper lotion potassium sulphate lotion Vioform cream or Quinolor ointment

ACNE URTICATA

This is an eruption of small wheals on the scalp face or elsewhere Excoriations often result (see Urticaria)

ACNE SCROFULOSORUM (see Cutaneous Tuberculosis)

ACNE AGMINATA (ACNITIS LUPOID PAPULAR TUBERCULIDE)

Clinical Picture—This is a papular eruption affecting the forehead eyelids nose and cheeks and sometimes the penis The papules are yellow and translucent giving a lupoid apple jelly appearance on diascopy The lesions are all at the same stage of development Necrosis subsequently occurs and when the scabs separate depressed scars are left

Ætiology and Pathology—The condition has been thought to be a tuberculide but the Mantoux reaction may show normergy or hypoergy to tuberculin and it has been suggested that the condition is a viride

to brine, pitch tar, organic chlorine compounds, paraffin or petroleum oils (cutting oils, greases, waxes) may cause or aggravate acne

Woollen underclothing should not be worn next to the skin

The acne patient should be encouraged to take outdoor exercise in all weathers The fine exfoliation that follows sun bathing is beneficial as is the flush that follows exposure to wind and rain

Infected acne may be improved with appropriate topical antibiotics and by staphylococcal toxoid injections

In those cases of acne in which emotional factors are relevant the control is difficult and psychiatric assistance is sometimes necessary The acne patient should be encouraged to mix with other young people and to have wide social activities

Local treatment —This mainly aims at bringing about a fine peeling of the skin For this purpose a weekly second degree exposure to ultra violet irradiation (enough to cause a branny peeling) is most helpful The carbon arc lamp is most efficacious but, if not available, good results can usually be obtained with the mercury vapour lamp Before giving either of these treatments to acne involving the trunk it is advisable to make a radiographic examination of the chest in order to exclude the presence of an asymptomatic focus of tuberculosis which might be activated by this treatment For more severe acne induratum, a third degree exposure (to cause coarse peeling) may be necessary

Medicaments for local application in acne should either be lotions or pastes Creams and ointments are likely to prove harmful Zinc sulphate lotion compound sulphur lotion and calamine lotion with 2 per cent of sulphur are all useful A flesh tinted paste will serve the double purpose of treatment and camouflage Resorcin and sulphur paste (tinted) is of reasonable cosmetic quality

The liberal use of soap and water and the avoidance of cream cosmetics should go hand in hand with the above treatment Many patients with acne vulgaris manipulate the lesions by squeezing in the hope that contents will be expressed and resolution hastened This undesirable habit is the cause of much funnel like scarring of the follicular orifices Manipulation should be limited to brisk friction with a face flannel or a soft nail brush

Carbon dioxide snow applications (1 to 3 seconds) to larger nodules are useful by bringing about a coarse peeling

Cystic swellings need puncture before giving this treatment

X-rays can be used with a view to bringing about some involution of the sebaceous glands in severe and resistant acne particularly if it is localised An exposure of 100 to 150 r repeated weekly up to a total of 600 r is a reasonable dosage Any cystic swellings should be punctured before this treatment is given On no account should more than two of such courses be given (total 1200 r) because above this level post irradiation atrophic changes are likely to occur

ACNE EXCORIÉE DES JEUNES FILLES

In this condition excoriations dominate the picture Comedones are usually but not always present and numerous excoriated papules and scars particularly at the forehead temples cheeks and chin

Acne excoriee indicates the presence of an emotional conflict and calls for psychological investigation and treatment Local treatment is ineffective unless the urge to pick the spots has been removed The best application is a flesh tinted paste for example titanium dioxide paste

ACNE IN INFANCY

This is rare but may occur in the following ways

(1) Newborn babies often have numerous small papulo-pustules on the face for

mentation The mouth is not affected Nikolsky s sign is negative and the Tzanck test shows blood cells particularly eosinophils but no acantholytic epidermal cells The administration of potassium iodide by mouth or a patch test with potassium iodide causes an increased vesiculation There is usually eosinophilia The general health suffers little if at all apart from the disturbing effects of the intense itching

Course and Prognosis—Dermatitis herpetiformis may persist for several years, with fluctuations after which it sometimes gets gradually milder and finally disappears Its onset and course is controlled to some extent by any emotional stresses to which the sufferer may be exposed The prognosis as regards life is good

Diagnosis is from other bullous eruptions erythema multiforme urticaria prurigo general pruritus and infestations The other bullous eruptions are in no way so itchy as dermatitis herpetiformis Pemphigus often affects the mouth and leaves extensive raw areas the patient being gravely ill In erythema multiforme bullosum itching is less the blisters are always within erythematous areas and excoriations are absent Urticaria is evanescent though possibly recurrent In prurigo lichenification and excoriation are the predominant features and vesicles are never seen In pruritus there may be scratch marks and excoriations but no vesicles In infestations there are scratch marks on the shoulders and around the waist and an examination of the scalp and underclothes should disclose the cause

Treatment—Sulphapyridine (but no other sulphonamide) acts as a specific in dermatitis herpetiformis with very few exceptions A dose of 1 g three times a day controls the itching and the development of vesicles within 24 to 36 hours After this the dose is reduced until the optimal level is found at which the symptoms are just controlled The addition of nicotinic acid 50 mg up to three times a day may enable a smaller dosage of sulphapyridine to be used Periodic total and differential white cell counts should be performed to detect drug leucopenia If the white cell count remains around 6000 per c mm the drug may be continued indefinitely without harm If the white cell count drops to 4000 per c mm or lower it is advisable to suspend the sulphapyridine for a time and to replace it by some other form of treatment Dapsone 50 mg daily is often as effective as sulphapyridine When taking this drug the patient should also be given ferrous sulphate tablets and vitamin B Fowler s solution in a dosage of 3 to 5 minims three times a day is often effective but it is best to revert to sulphapyridine or to dapsone as soon as the white cell count permits because of the long term toxic effects that may result from the use of Fowler s solution

Antibiotics sometimes help and sometimes aggravate dermatitis herpetiformis and their trial is only justified when other means fail When they are used the patient should be kept under close observation so that treatment can be suspended at once if untoward symptoms develop

General ultra violet irradiation sometimes seems to relieve the itching Phenobarbitone is also useful in the interim between courses of sulphapyridine or dapsone but bromides are contraindicated because like iodides they may aggravate the condition

Local applications that may help include 1 per cent. of phenol in calamine lotion and 2 per cent of solution of coal tar in Lassar s paste Sodium bicarbonate baths (4 oz in 25 gallons) may prove soothing

HERPES GESTATIONIS

This is a form of dermatitis herpetiformis affecting pregnant women usually in the third trimester It may recur in subsequent pregnancies Relief usually but not always occurs after delivery

Treatment is complicated in that both sulphapyridine and Fowler s solution are undesirable because of the pregnancy Dapsone may be used or recourse had to

Histologically there is a tuberculoid pattern with central caseation and a surrounding inflammatory infiltrate

Course and Prognosis —The lesions are resistant to treatment by antituberculous drugs but tend to undergo spontaneous resolution after several months leaving scars

Treatment is supportive and nonspecific

CHRONIC BULLOUS ERUPTIONS

The chronic bullous eruptions are a group of reactions of unknown cause, the recognition of which is nevertheless most important because of their differing prognoses and treatments In their differentiation reliance has to be placed on the history and physical signs and in particular on the presence or absence of Nikolsky s sign The Tzanck test also is a simple and useful diagnostic procedure

Nikolsky's sign can be demonstrated in two ways If there is an intact bulla an attempt is made to push this along in the skin with one thumb, while anchoring the adjacent skin with the other hand Nikolsky s sign is positive if the bulla can be moved along in the skin The other method is to apply tangential stress to the apparently normal skin The skin over the collarbone or tibia is anchored with the left thumb and forcible lateral pressure is applied with the right thumb The sliding off of the superficial layers indicates a positive Nikolsky s sign The sign is positive in pemphigus vulgaris pemphigus vegetans pemphigus foliaceus pemphigus erythematodes, pemphigoid benign familial pemphigus and epidermolysis bullosa It is negative in dermatitis herpetiformis and in erythema multiforme

The Tzanck test is performed by removing the roof and scraping the floor of a bulla The material thus obtained is spread on a slide stained and examined under the microscope for acantholytic cells (epidermal cells which have lost their prickles) Alternatively, lateral stress may be applied to a portion of skin and biopsy subsequently performed The Tzanck test is positive if slit like clefts are apparent within the epidermis and if within them single acantholytic cells or groups of them are seen

DERMATITIS HERPETIFORMIS (DUHRING S DISEASE)

Dermatitis herpetiformis is a disorder in which grouped itchy vesicles and small bullæ arise on normal or reddened skin

Ætiology and Pathology —The cause is unknown a virus cause is suspected It is most common between the ages of 30 and 50 and is rare in early adult life and in childhood There is an excessive susceptibility to the blister producing influences of potassium iodide both by its ingestion and by its topical application

Histologically the bullæ are at the epidermo dermal junction they tend to be oval in shape when seen in sections they contain blood cells with many eosinophils but no abnormal epidermal cells There is an infiltrate of inflammatory cells around the bullæ The overlying epidermis shows evidence of scratching with loss of tissue a nonspecific infiltrate including some eosinophils and perhaps some patchy spongiosis and irregular excesses of melanin pigmentation

Clinical Picture —The patient complains of an intensely itchy eruption which though often widespread shows a marked tendency to grouping The sites most commonly affected are the shoulder blades the elbows the buttocks and genitalia and the knees but no area is immune and the face may be involved The eruption is polymorphic The individual lesions are flaccid or tense millet seed sized vesicles arising from skin which may be apparently normal or reddened Owing to the severe itching it is rare to see many intact vesicles and the physical signs usually consist more of excoriated and scabbed erythematous papules erosions scars and patchy pig

PEMPHIGUS FOLIACEUS AND PEMPHIGUS ERYTHEMATODES

These are forms of pemphigus in which exfoliation is the most prominent feature bullæ rarely being seen because they are superficial and easily ruptured The course is irregular but usually somewhat more benign than pemphigus vulgaris Remissions and relapses occur It is uncertain whether the condition can develop into pemphigus vulgaris

Pathology—The cellular disruption is at the granular cell layer The overlying cells become detached with the result that on section blisters are not seen but the granular layer is either exposed to the surfaced or covered by loosely attached groups of horny cells

Clinical Picture and Differential Diagnosis—In pemphigus foliaceus the picture resembles erythroderma perhaps with some econdary infection but Nikolsky s sign is positive in pemphigus foliaceus and negative in erythroderma There is cru ting and a tendency to wartiness with pigmentation In pemphigus erythema todes (Senear Usher syndrome) the condition resembles infective dermatitis because the superficial lesions become secondarily infected or with single or few lesions on the face there may be a resemblance to lupus erythematosus but the moistness of the lesions and the looseness of the overlying skin cast doubt on the diagnosis of lupus erythematosus

Nikolsky's *sign is positive There is a variable degree of general disability*

Course and Prognosis—The natural course is a slow worsening with remissions *and recrudescences and a fatal outcome usually from some infective complication*

Treatment is as for pemphigus vulgaris (*q v*) with corticotrophin or cortisone and antibiotics Blood or plasma transfusions are usually unnecessary because the loss of body fluid is much less than in pemphigus vulgaris When the secondary infection is under control calamine liniment may be applied

SENILE DERMATITIS HERPETIFORMIS OR PEMPHIGOID

An eruption of tense bullæ often with considerable erythema around with much itching occurring in the seventh or eighth decades and sometimes ending fatally

Ætiology and Pathology—The cause is unknown

The bullæ are at the epidermo dermal junction and contain blood cells including many eosinophils They are oval when seen in sectional view

Clinical Picture—Large tense bullæ some containing straw coloured fluid others containing blood or even pus are present in the skin particularly on the limbs The mucous membranes of the mouth are sometimes affected with blisters and raw areas but the vermilion surfaces of the lips escape There is intense itching but less constitutional upset than in pemphigus vulgaris Nikolsky s sign is positive but the Tzanck test shows eosinophil and other blood cells but no acantholytic cells The bullæ do not rupture easily and if they are broken they tend to heal and do not spread spontaneously as in pemphigus vulgaris Small white cysts (milia) may form in the process of healing Serum protein and electrolytic changes are minimal

Course and Prognosis—The natural course is chronicity with occasional re missions The prolonged course with loss of sleep from itching and secondary infection may lead to death

Diagnosis from erythema multiforme may be difficult In erythema multiforme Nikolsky s sign is negative and spontaneous resolution occurs in a few days or weeks

Pemphigus vulgaris differs from pemphigoid by its more flaccid and easily rup tured blisters with severe involvement of the mouth and lips and a heavy loss of electrolytes and protein Senile dermatitis herpetiformis differs from dermatitis herpetiformis in its larger tense bullæ positive Nikolsky s sign muco al involvement and more serious course

Treatment is as for pemphigus (*q v*) with corticotrophin or cortisone After

symptomatic relief with phenobarbitone or promethazine hydrochloride until the time of delivery

PEMPHIGUS VULGARIS

A bullous disorder with an irregular course, often ending fatally In the flexures it forms vegetations (pemphigus vegetans)

Ætiology and Pathology—The cause is unknown essentially there is a lack of cohesion between the epidermal prickle cells The malady usually occurs after the age of 40 and Jews are especially liable to be affected

Histologically there are slit like clefts within the stratum mucosum just above the stratum germinatum and acantholytic cells are seen within the clefts In section the extremities of the clefts are acute as opposed to the obtuse clefts seen in dermatitis herpetiformis

Clinical Picture—Large and small flaccid bullæ are present on seemingly normal areas of skin Many ruptured bullæ are seen with extensive red raw areas from which considerable loss of serum occurs These raw areas tend to spread peripherally and show no tendency to heal spontaneously Itching is slight or absent The general health steadily deteriorates Secondary infection is common particularly in the flexures where malodorous soft moist, warty elevations or vegetations develop The malady may at first be localised but ultimately the whole surface may be patchily affected At pressure sites such as the elbows scapulæ sacrum buttocks and heels deep sores are liable to form The mucous membranes of the mouth vulva and penis are usually affected with considerable distress to the patient The vermilion surface of the lips and the mucous surfaces of the tongue cheeks and roof and floor of the mouth are extensively denuded giving an appearance of rawness covered by a white exudate and with loose tags of epidermis at the edges Nikolsky s sign and the Tzanck test are positive The serum proteins are often markedly diminished (particularly the albumin) owing to loss of body fluids from the extensive oozing raw areas There is severe hypochromic anæmia and salt depletion Sodium chloride and calcium depletion also occur but the serum potassium may be raised Ulceration of the mouth interferes with swallowing and may further weaken the patient from nutritional deficiency

Course and Prognosis—The natural course is one of worsening with occasional spontaneous remissions usually followed by fresh outbreaks of increased severity ultimately leading to death from general infection and pneumonia complicated by protein and electrolytic deficiencies This gloomy picture has been greatly improved since the introduction of corticotrophin and cortisone

Diagnosis from other bullous eruptions is made with certainty from a consideration of the physical signs and the results of the Tzanck test

Treatment—The first essential is nursing care of the highest standard Corticotrophin intramuscularly in a dose of up to 50 mg every 6 hours usually leads to a remission The dose is then reduced to the minimal maintenance level The mucous lesions do not respond so well as the skin lesions The latter heal well with deep pigmentation When the patient becomes ambulant cortisone orally is more convenient in the smallest dose consistent with relief This treatment may have to be combined with an antibiotic to combat any infection that is present

Whole blood or plasma transfusions are useful but they cannot in themselves replace the deficiency of albumin and an adequate diet high in protein content, must be given Nasal feeding may be necessary The mouth must be kept as clean as possible with normal saline or glycerin and thymol

For the infected skin chlortetracycline ointment is useful and when the lesions are clean tulle gras applications are comforting Some prefer a powder bed the patient lying in sheets heavily sprinkled with boric talc powder

bear no relation to treatment seasons or any other known cause Regarding length of life the prognosis is good

Diagnosis—From infective dermatitis the condition is recognised by its chronicity and by the characteristic histology

Treatment—There is no effective treatment The lesions should be covered with calamine liniment to which may be added 1 per cent of ichthammol or 0 1 per cent of pyrogallol Antibiotics may be used for any serious degree of secondary infection Clothing should be soft and smooth and loosely fitting A dusting powder containing zinc oxide and zinc stearate may by giving slip help to prevent the development of lesions

EPIDERMOLYSIS BULLOSA

This inherited malady occurs in two forms the simple and the dystrophic The skin is vulnerable to minor traumata and to sunlight

Ætiology and Pathology—The cause is a genetic fault

The histology differs in the two forms In the simple form clefts occur in the epidermis but in the dystrophic form they are in the dermis and scarring and loss of tissue often result with the formation of epidermal cysts

Clinical Picture—In the simple form the infant is noticed to blister easily at sites of trauma especially the hands and feet elbows and knees shoulder and buttocks In milder forms this phenomenon may not be apparent until later in life and serious blistering may only be noticed when the individual starts soldiering

In the dystrophic form the disruption of the dermis is so severe that scarring and deformity often result In particular the nails are likely to be shed and the new nails are dystrophic and irregular Ectodermal defects of the hair and teeth may also be present and erosions occur on mucous surfaces as well as on the skin

Course and Prognosis—The course is uninterrupted and there are no remissions The condition interferes considerably with the patient s activities

Treatment—There is no effective treatment The aim should be the avoidance of traumata likely to cause blistering Special care is necessary in the choice of clothing particularly shoes and the sufferer cannot join in many of the activities usually indulged in by the young Blisters should be dealt with by careful puncture and antibiotics applied if infection occurs

SCLERODERMA AND ALLIED CONDITIONS

Sclerosis is a condition in which collagen undergoes inflammatory fibrotic changes proceeding to a terminal atrophic phase If the skin seems to be the only organ affected the term scleroderma is appropriate but when one or more internal organs are affected the term systemic sclerosis is more suitable

CIRCUMSCRIBED SCLERODERMA

Clinical Picture—Circumscribed scleroderma (morphœa) presents as an itchy round oval or irregular firm pale or skin coloured smooth candle wax like plaque with a lilac halo There may be one or several of such lesions and when numerous there is a marked tendency to symmetry A variant is morphœa guttata

Ætiology and Pathology—The cause is unknown Adults are affected more than children and women more than men

Histologically there is an early inflammatory stage in which the collagen bundles are swollen homogeneous and separated by œdema the fat and elastic tissue degenerate or destroyed There is a lymphocytic infiltrate Later the infiltrate diminishes and the collagen of the dermis is seen to be thickened and condensed The blood

obtaining a remission with intramuscular corticotrophin the ambulant patient can be treated with gradually reduced doses of cortisone until in some cases the drug can be withdrawn and recurrence does not occur In others mild or severe recrudescences necessitate further treatment with corticotrophin Local treatment consists of aseptic puncture and collapse of the large tense bullæ and suitable antibiotic or emollient dressings

BENIGN PEMPHIGUS OF THE MUCOUS MEMBRANES (OCULAR PEMPHIGUS)

A bullous eruption in which the eyes and mouth are mostly affected and the skin slightly or not at all

Pathology—The blisters are at the epidermo dermal junction there is no acanthosis but a heavy inflammatory infiltrate and later fibrosis

Clinical Picture—The conjunctivæ become inflamed and fibrous adhesions form between the palpebral and ocular surfaces or between the upper and lower palpebral surfaces The conjunctival sacs become shallow and the palpebral fissures narrow and the eyeballs limited in their range of movement The cornea may be damaged by entropion xerosis or pannus with loss of vision Vesicles form in the mouth and by coalescence form large red denuded areas The vermilion surface of the lips escapes but the mouth may be narrowed by adhesions Lesions may form anywhere in the mouth nose or throat in the œsophagus causing dysphagia on the glans penis or prepuce causing phimosis or on the vulva or vagina causing narrowing The skin of the scalp or face is affected in about half the patients with erythema flaccid bullæ and erosions going on to scarring

Course and Prognosis—The malady is slowly progressive with remissions and recurrences

Diagnosis is from pemphigus vulgaris pemphigoid, severe erythema multiforme and aphthosis including Behcet s syndrome

In pemphigus the lesions are in the epidermis and the vermilion surfaces of the lips are often affected In pemphigoid the eyes usually escape and the skin lesions which predominate consist of large tense bullæ In severe erythema multiforme the onset is abrupt, the patient is a child or young adult and the skin involvement is extensive In Behcet s disease there are erosions and ulceration of the eyes mouth and genitalia often with some destruction of tissue

Treatment—Cortisone eye drops are invaluable and corticotrophin or cortisone may help to alleviate the other manifestations For the mouth a bland mouth wash should be prescribed

BENIGN FAMILIAL PEMPHIGUS (OF GOUGEROT AND HAILEY HAILEY)

This is a chronic erosive condition of friction sites occurring in many members of the same family benign in its course and with a tendency to spontaneous remissions

Ætiology and Pathology—This inherited malady is possibly a bullous variant of dyskeratosis follicularis

Histologically there is acantholysis the detachment occurring in the stratum mucosum

Clinical Picture—Benign pemphigus resembles a very resistant infective dermatitis The lesions are flexural or at sites of friction such as the *collar line* axillary folds and groins and they consist of erosions covered by greasy *scaling* The patient complains of a tendency to chafing of the skin at sites of pressure from clothes and there is a history of a similar condition in other members of the family

Course and Prognosis—The course is chronic with occasional remissions which

bear no relation to treatment seasons or any other known cause Regarding length of life the prognosis is good

Diagnosis —From infective dermatitis the condition is recognised by its chronicity and by the characteristic histology

Treatment —There is no effective treatment The lesions should be covered with calamine liniment to which may be added 1 per cent of ichthammol or 0 1 per cent of pyrogallol Antibiotics may be used for any serious degree of secondary infection Clothing should be soft and smooth and loosely fitting A dusting powder containing zinc oxide and zinc stearate may by giving slip help to prevent the development of lesions

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In the dystrophic form the disruption of the dermis is so severe that scarring and deformity often result In particular the nails are likely to be shed and the new nails are dystrophic and irregular Ectodermal defects of the hair and teeth may also be present and erosions occur on mucous surfaces as well as on the skin

Course and Prognosis —The course is uninterrupted and there are no remissions The condition interferes considerably with the patient s activities

Treatment —There is no effective treatment The aim should be the avoidance of traumata likely to cause blistering Special care is necessary in the choice of clothing particularly shoes and the sufferer cannot join in many of the activities usually indulged in by the young Blisters should be dealt with by careful puncture and antibiotics applied if infection occurs

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Ætiology and Pathology —The cause is unknown Adults are affected more than children and women more than men

Histologically there is an early inflammatory stage in which the collagen bundles are swollen homogeneous and separated by œdema the fat and elastic tissue degenerate or destroyed There is a lymphocytic infiltrate Later the infiltrate diminishes and the collagen of the dermis is seen to be thickened and condensed The blood

obtaining a remission with intramuscular corticotrophin the ambulant patient can be treated with gradually reduced doses of cortisone until in some cases the drug can be withdrawn and recurrence does not occur In others mild or severe recrudescences necessitate further treatment with corticotrophin Local treatment consists of aseptic puncture and collapse of the large tense bullæ and suitable antibiotic or emollient dressings

BENIGN PEMPHIGUS OF THE MUCOUS MEMBRANES (OCULAR PEMPHIGUS)

A bullous eruption in which the eyes and mouth are mostly affected and the skin slightly or not at all

Pathology—The blisters are at the epidermo dermal junction there is no acanthosis but a heavy inflammatory infiltrate and later fibrosis

Clinical Picture—The conjunctivæ become inflamed and fibrous adhesions form between the palpebral and ocular surfaces or between the upper and lower palpebral surfaces The conjunctival sacs become shallow and the palpebral fissures narrow and the eyeballs limited in their range of movement The cornea may be damaged by entropion xerosis or pannus with loss of vision Vesicles form in the mouth and by coalescence form large red, denuded areas The vermilion surface of the lips escapes but the mouth may be narrowed by adhesions Lesions may form anywhere in the mouth nose or throat in the œsophagus, causing dysphagia, on the glans penis or prepuce causing phimosis or on the vulva or vagina causing narrowing The skin of the scalp or face is affected in about half the patients with erythema flaccid bullæ and erosions going on to scarring

Course and Prognosis—The malady is slowly progressive with remissions and recurrences

Diagnosis is from pemphigus vulgaris pemphigoid severe erythema multiforme and aphthosis including Behcet s syndrome

In pemphigus the lesions are in the epidermis and the vermilion surfaces of the lips are often affected In pemphigoid the eyes usually escape and the skin lesions which predominate consist of large tense bullæ In severe erythema multiforme the onset is abrupt the patient is a child or young adult and the skin involvement is extensive In Behcet s disease there are erosions and ulceration of the eyes mouth and genitalia often with some destruction of tissue

Treatment—Cortisone eye drops are invaluable and corticotrophin or cortisone may help to alleviate the other manifestations For the mouth a bland mouth wash should be prescribed

BENIGN FAMILIAL PEMPHIGUS (OF GOUGEROT AND HAILEY HAILEY)

This is a chronic erosive condition of friction sites occurring in many members of the same family benign in its course and with a tendency to spontaneous remissions

Ætiology and Pathology—This inherited malady is possibly a bullous variant of dyskeratosis follicularis

Histologically there is acantholysis the detachment occurring in the stratum mucosum

Clinical Picture—Benign pemphigus resembles a very resistant infective dermatitis The lesions are flexural or at sites of friction such as the collar line axillary folds and groins and they consist of erosions covered by greasy scaling The patient complains of a tendency to chafing of the skin at sites of pressure from clothes and there is a history of a similar condition in other members of the family

Course and Prognosis—The course is chronic with occasional remissions which

sorption of the tufts of the terminal phalanges and there may be subcutaneous deposits of calcium Radiography of the chest may show reticulation due to pulmonary fibrosis or areas of pneumonia due to aspiration from the œsophagus there may be hypertrophy of the right side of the heart and the electrocardiogram may be abnormal Radiological investigation of the gastro intestinal tract is often abnormal in the œsophagus fibrous stricture dilatation absence of peristalsis and hiatus hernia have been described diminished peristalsis dilatation and diverticula have been seen in the small and large intestine

Course and Prognosis—Rarely there is rapid evolution of the disease with death in a few months More usually the disease is slowly progressive without remissions with increasing disability from Raynaud s phenomenon painful indolent fissures of the fingers limitation of movement of the fingers wrists elbows and shoulders increasing dyspnœa and perhaps dysphagia Death occurs in 5 to 10 years from inhalation broncho pneumonia heart failure or renal failure The disease may become arrested leaving the patient with residual deformities due to fibrosis

Diagnosis—In the early stages the aching and swelling of the fingers may suggest rheumatoid arthritis and Raynaud s phenomenon has to be distinguished from Raynaud s disease

Pulmonary involvement may be confused with bronchiectasis pigmentation with Addison s disease and œsophageal involvement with cardiospasm

Treatment—Local applications such as compound tincture of benzoin in lanoli may be necessary for the painful fissures of the fingers Raynaud s phenomenon should be treated in the same way as Raynaud s disease if it is severe cervical sympathectomy is justifiable although it has no influence on the course of the disease

Corticotrophin and cortisone may produce a temporary improvement in the œdema tous stage but has no effect on the fibrotic lesions and it does not appear to have any effect on the ultimate prognosis

DERMATOMYOSITIS

Ætiology—The cause is unknown Males and females are equally affected the disease usually starts between the ages of 20 and 40 Some cases have been associated with carcinoma of the lung and other organs

Pathology—In the skeletal muscles there is parenchymal degeneration with an interstitial inflammatory reaction there is proliferation of nuclei of the muscle fibres and loss of the normal cross striations in the interstitial tissue there is a variable infiltration with lymphocytes histiocytes plasma cells and fibroblasts Later there is replacement fibrosis of the muscles Similar changes may be found in the myocardium In the dermis the collagen fibres may be swollen and homogeneous and there is a perivascular infiltration with lymphocytes and other cells

Clinical Picture—The onset is usually insidious but may be acute The early symptoms are muscular pain and weakness or subcutaneous œdema and erythema Occasionally Raynaud s phenomenon is the first symptom There may be generalised involvement of skeletal muscles from the start or the disease may begin in the limbs and spread to the trunk The neck shoulder and pelvic girdle muscles are most affected The muscles are painful tender and weak they feel indurated and later hard and fibrous

There is limitation of movement because of inability of the muscles to stretch The tendon jerks are diminished or absent Dysphagia dysphonia and dyspnœa are common from involvement of the pharynx larynx intercostal muscles and dia phragm Facial weakness and diplopia may be found

Skin changes are rarely absent and may be persistent or transient The com monest change is a firm subcutaneous œdema which may be generalised but is usually confined to the face and limbs There may be a diffuse mottled purple

vessels of the dermis and hypoderm show similar changes The pilosebaceous follicles disappear but the sweat glands usually perist

Course and Prognosis—Clinically the lesions may cease to itch and end in moderately atrophic plaques This form, whether solitary or multiple seems to be unrelated to systemic sclerosis In the severest forms bullæ may develop owing to lymph stasis

Diagnosis is from lichen sclerosus et atrophicus, vitiligo paraffinoma, leprosy (*q v*)

Treatment—There is no specific treatment A bland application such as unguentum aquosum to make up for the secondary sebaceous deficiency is often comforting Sedatives may be required for severe itching

SYSTEMIC SCLEROSIS

Ætiology—The cause is unknown The disease occurs almost exclusively in women and usually starts before the age of 40

Pathology—The changes in the skin are similar to those in circumscribed scleroderma In the gut there are areas where the muscularis is replaced by fibrous tissue There may be invasion of the myocardium and skeletal muscles by connective tissue with atrophy of muscle fibres The alveolar walls in the lungs may be infiltrated by fibrous tissue, and the capillary loops of the kidney often show fibrinoid degeneration

Clinical Picture—This is usually a very slowly progressive disease in which the early manifestations are due to involvement of the skin and subcutaneous tissue later there is often evidence of visceral involvement The earliest changes in the skin are thickening and non pitting œdema but this stage may be absent Later there is induration so that the skin cannot be pinched up and finally there is atrophy involving also the subcutaneous tissue when the skin is bound down to the deeper structures

The onset is usually insidious, starting in the hands with Raynaud s phenomenon or aching stiffness and swelling of the fingers If Raynaud s phenomenon is the first symptom it is usually followed in a few weeks by swelling and limitation of movement but occasionally there is an interval of many years There is a gradual extension over several years to the forearms face and chest Later the feet and legs may be affected and rarely the whole body The onset is sometimes more rapid the evolution taking about a year Rarely the disease may start in the face and trunk sparing the hands

The fingers are pointed with wasting of the pulps of the terminal phalanges the nails curved the skin is shiny thin and tightly bound to the deep fascia causing limitation of movement there may be painful fissures and ulcers and areas of superficial gangrene The face is expressionless with loss of the natural creases the nose is pointed, the mouth pinched and the lips thin and puckered The skin of the limbs and trunk is thickened and difficult to pinch up There is limitation of movement of the joints within the affected area There is often diffuse dark brown pigmentation of the skin and sometimes telangiectasia Subcutaneous nodules of calcinosis may be found, especially in the fingers and near the elbow joints The skeletal muscles may be weak and wasted

Visceral involvement is often discovered by special investigation in the early stages and as the disease progresses symptoms may be produced cough and dyspnœa from pulmonary lesions and dysphagia and constipation from alimentary lesions are common Heart failure may be caused by myocardial lesions or by the pulmonary fibrosis The spleen and lymph glands may be enlarged Albuminuria may be found but renal failure is rare

Special investigations—Radiography of the hands almost invariably shows re

sorption of the tufts of the terminal phalanges and there may be subcutaneous deposits of calcium Radiography of the chest may show reticulation due to pulmonary fibrosis or areas of pneumonia due to aspiration from the œsophagus there may be hypertrophy of the right side of the heart and the electrocardiogram may be abnormal Radiological investigation of the gastro intestinal tract is often abnormal in the œsophagus fibrous stricture dilatation absence of peristalsis and hiatus hernia have been described diminished peristalsis dilatation and diverticula have been seen in the small and large intestine

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erythema, not necessarily coextensive with the œdema or the muscles involved, which is usually confined to the face and limbs Later there may be areas of pigmentation and atrophy of the skin, usually on the backs of the hands elbows knees or face Stomatitis with œdema, redness and crusted erosions, alopecia and subcutaneous calcinosis may be found Less common features are Raynaud s phenomenon, par æsthesiæ of the fingers and enlargement of the spleen, liver and lymph glands The temperature is usually normal or only slightly raised

Special investigations —Creatinuria is constantly found The radiograph of the chest may show enlargement of the heart and the electrocardiogram is occasionally abnormal Albuminuria is found in about half the cases

Course and Prognosis —The course is often indicated by the onset when the onset is acute the course is likely to be rapidly fatal, when the onset is insidious complete or partial remission is probable The muscular weakness progresses, steadily or with remissions in extent and degree About half the patients die in a few months to 5 years of broncho pneumonia or respiratory paralysis Occa ionally death is due to heart failure At any stage the disease may become arrested or regress leaving permanent incapacity from limitation of movement and residual changes in the skin of sclerodermatous thickening A few patients recover completely

Diagnosis —The skin lesions have to be distinguished from scleroderma dis seminated lupus erythematosus and poikiloderma atrophicans vasculare Oedema of the face with muscle pain may mimic trichiniasis If weakness is the outstanding feature polyneuritis and myasthenia gravis have to be excluded

Treatment —Dysphagia and respiratory paralysis are the chief cases of death, they may require treatment by gastric intubation pharyngeal suction and artificial respiration as in acute anterior poliomyelitis

Physiotherapy is necessary to prevent and correct deformities Corticotrophin or cortisone may arrest the progression of the disease and produce a complete remission

SCLEREDEMA ADULTORUM (BUSCHKE)

This is a condition in which œdema and induration develop in the skin and hypoderm usually after a period of fever It starts on the head and spreads over the neck and trunk Serous effusion into the pericardium, pleura and joints may occur but the disorder is self limited, clearing up after a few months to a year

Ætiology and Pathology —The cause is unknown

Histologically, there is swelling of the collagen with interstitial œdema and a slight perivascular inflammatory infiltrate

Treatment is symptomatic and supportive

SCLEREMA

Two types of this malady occur

In the *generalised form* (sclerema neonatorum) the skin all over the body is waxy, hard cold and pale or livid The temperature is subnormal Death may occur within the first week or two after birth but milder forms occur from which the infant may recover

Ætiology and Pathology —The olein content of the fat is diminished, giving the body fat a higher melting point with the result that solidification occurs at ordinary temperatures

Histologically there is crystallisation of the hypodermal fat, with an inflammatory infiltrate of foreign body giant cell type ending in fibrosis

In the *nodular form* (lipophagic granuloma) the histological features are the same but the process is localised and self limited the hard areas disappearing *in a few* months This form may affect adults and clinically resembles morphœa or paraffinoma (*q v*)

Diagnosis is usually made on histological grounds
Treatment —There is no effective treatment

ATROPHY OF THE SKIN

This occurs in the ageing skin but to a greater extent in areas exposed to light than in those not so exposed In its simplest form in covered areas there is thinning and loss of elasticity giving a yellowish wrinkled and tissue papery appearance and texture Histologically there is thinning of the epidermis with a flattened epidermo dermal junction The dermis is also thin and shows collagenous atrophy the hypo dermic fat is also less marked At sites exposed to light degeneration of the collagen and of the elastin are more marked both becoming basophilic and the latter being fragmented and forming irregular clumps

Senile elastosis (peasants skin) is a leathery thickening with marked furrowing occurring especially on the back of the neck (cutis rhomboidalis nuchæ) Histologic ally there is an apparent increase of elastic tissue with degenerative clumping swelling and fragmentation of its fibres

Glossy skin (atrophoderma neuriticum) occurs in conditions such as leprosy where there may be interference with the nerve supply to a part

Pressure atrophy occurs at sites of continuous pressure for example under the pads of trusses

Vulvar atrophy (senile atrophic vulvitis) may cause stenosis of the vaginal orifice (kraurosis vulvæ) The mucosa is dry shiny smooth and pale or there may be patchy telangiectasia and pigmentation Leucoplakia (mucosal hyperkeratosis) and even squamous carcinoma may be the final outcome Histologically the epidermis is thinned the collagen and elastin degenerated the blood vessels sclerosed and there may be lymphœdema of the upper dermis even going on to bulla formation

Macular atrophy (round and oval atrophic patches particularly on the trunk) may be an idiopathic condition or a manifestation of past secondary syphilis It may also occur in leprosy lupus erythematosus as a later stage of morphœa or as a part of the condition known as acrodermatitis chronica atrophicans The idiopathic form has two varieties one preceded by inflammation (Jadassohn) the other (Schwenınger Buzzi) having no earlier inflammatory stage Diagnosis is from von Recklinghausen s disease In both conditions there are hernia like orifices and grape like swellings in the skin but in macular atrophy the other features of von Recklinghausen s disease (*q v*) are absent

Macular and striate atrophy is seen in the condition sometimes called striæ cutis distensæ or striæ gravidarum This linear form of atrophy chiefly affects the breasts abdomen and thighs of pregnant women but is also seen in Cushing s syndrome and in some fat young people of either sex It is believed that in all cases an endo crine factor is responsible distension by itself not causing this condition as is clear from observation of fat persons The atrophic areas may be pink or purple when fresh skin coloured and more fibrotic when older

Atrophoderma reticulatum is a condition of pinhead sized atrophic ridges separ ated by narrow ridges of normal skin It occurs on the cheeks is of unknown cause and is untreatable except by cosmetic camouflage

Acrodermatitis chronica atrophicans is a disease which is rare in the British Isles and much more common on the Continent of Europe As the name implies it affects mainly the extremities where the skin is brownish red and swollen later becoming atrophic and wrinkled with subcutaneous veins clearly visible One or more limbs may be affected Usually fibrotic nodules and bands are present over the subcutaneous surface of the ulna or of the tibia Histologically there is hyperkeratosis thinning of the rest of the epidermis and œdema and degeneration of the collagen with a

erythema, not necessarily coextensive with the œdema or the muscles involved which is usually confined to the face and limbs Later there may be areas of pigmentation and atrophy of the skin, usually on the backs of the hands elbows, knees or face Stomatitis with œdema redness and crusted erosions, alopecia and subcutaneous calcinosis may be found Less common features are Raynaud s phenomenon, par æsthesiæ of the fingers and enlargement of the spleen liver and lymph glands The temperature is usually normal or only slightly raised

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are present and there is extensive atrophic and pigmented scarring over the elbows and knees Treatment is protective only

HYPERTROPHY OF THE SKIN

A corn (clavus) is a localised reactive hypertrophy the result of intermittent pressure and friction Histologically there is a dense hyperkeratosis with an acuminate downgrowth which presses the stratum mucosum down towards the dermis The stratum mucosum becomes thinned and atrophic Under the dermis there is often a bursa—a lymph space containing serous fluid Abacterial or bacterial inflammation may occur the latter sometimes with suppuration Corns most commonly occur on the upper surfaces of the toes particularly the small toes Sometimes they occur between the toes and owing to maceration are known as soft corns In this situation exostosis and fungous infection should be excluded as the cause Diagnosis is from warts by the fact that the latter either have a papillated surface or at least show a break in continuity of the epidermal lines of the skin Plantar warts may become buried under an hyperkeratotic cap Prevention is the ideal by suitable footwear Treatment consists of well fitting shoes and hose and paring of the excessive horny matter A salicylic acid plaster previously applied renders this procedure easier Recurrence is likely unless further pressure or friction is avoided

Callosities are diffuse thickenings of the horny layer without downgrowths such as occur with corns Callosities are due to excessive weight bearing as in obesity or from unnatural stresses as in pes planus They may also arise from roughened shoe linings and at innumerable sites in different occupations from intermittent friction and pressure (for example in gardeners boatmen housewives cobblers etc etc as occupational stigmata) Bursæ may form beneath the thickened firm inelastic skin which has a yellowish dirty appearance with a shelving edge and is painless Callosities are liable to undergo fissuring from which infection may result

Tylosis is a congenital hyperkeratosis of the palms and soles dominant in its inheritance The hard thickened skin cracks easily in the winter and becomes macerated and offensive in the summer The condition can be alleviated by 5 per cent salicylic acid ointment

Keratoderma climactericum affects the palms soles and heels and sometimes the knees of menopausal women usually obese There is much horny thickening at these sites and painful fissures tend to form around the heels Treatment is by œstrogens by mouth and salicylic acid ointment 2 to 5 per cent locally It is advisable to reduce the patient in weight by a stone or two in the course of a few months if possible

Keratoderma punctatum occurs in two forms one hereditary but occurring in early life the other apparently acquired and related to keratin stimulants operating around the sweat ducts On the palms (and sometimes on the soles) are discrete conical or rounded excresences of dense keratin with central puncta The condition is resistant to treatment but a 5 per cent salicylic acid ointment may help to soften the lesions

Arsenical keratosis (due to the ingestion of Fowler s solution) affects the palms with pinhead lesions although the soles may show larger excrescences Dirty grey keratoses and basal cell carcinomata may be present on the trunk and there may be raindrop depigmentation and pigmentation

Keratoderma blenorrhagica is an hyperkeratotic condition of the palms and soles and of the skin around and beneath the nails in which thick limpet like scaling and crusting occurs The condition is accompanied by urethritis polyarthritis and conjunctivitis The urethritis may be gonococcal or nonspecific Local treatment is with keratolytics

Porokeratosis of Mibelli is a congenital hyperkeratosis affecting in particular the

band like infiltrate of lymphocytes under the epidermis but separated from it by a thin band of relatively normal collagen There is also a perivascular infiltrate The hair papillæ and sebaceous glands are atrophic but the sweat glands survive under the thinned dermis The hypodermic fat is atrophic The cause of the malady is unknown It goes on from an early inflammatory and swollen stage to a later atrophic stage but it has no effect on length of life Diagnosis is from the main succulente of syringomyelia (by the absence of neurological signs), from erythromelalgia (by the absence of pain and warmth) Treatment is empirical Systemic penicillin has a reputation for bringing about an early remission

Poikiloderma —This is a condition of the skin in which telangiectasia pigmentation depigmentation and atrophy are intermingled It is an atrophic precancerous process

Ætiology and Pathology —Poikiloderma occurs after excessive solar or X irradiation It also occurs in an idiopathic form (poikiloderma vasculare atrophicans of Jacobi Lane) which may terminate in cutaneous reticulosis with tumour formation Poikilodermato myositis is an atrophic end stage of certain cases of dermatomyositis

The epidermis is atrophic and statically dilated blood vessels are present in the atrophic dermis

Course and Prognosis —All cases have to be watched for the development of keratoses or squamous carcinomata, or in the idiopathic form for reticulosis or mycosis fungoides

Diagnosis —The irradiation forms are usually easy to recognise from the history and situation The idiopathic form may occur with lichenoid papules on the trunk and with parapsoriasis like patches in addition to the poikiloderma

Treatment is by bland local applications for example hydrous ointment, and by appropriate action if malignancy occurs For cosmetic purposes the telangiectasia may be lessened by a touch with the galvano cautery or a suitable cover cream may be applied to mask the lesion

Poikiloderma atrophicans vasculare (Jacobi Lane) —This is a rare disorder of lichenoid papules with poikiloderma (pigmentation depigmentation telangiectasia and atrophy) The skin is dry and itchy The disorder is slowly progressive and may end in cutaneous reticulosis with tumour formation

Diagnosis is from radiodermatitis systematised lupus erythematosus and dermato myositis In radiodermatitis there is a history of irradiation in lupus erythematosus (*q v*) there are cytological and serological changes and in dermatomyositis there are muscle pains and creatinuria

Lichen sclerosus et atrophicus (see p 1279)

Pseudo xanthoma elasticum —This is a congenital abnormality consisting of a defect of the elastic tissue in the skin of the elastic membrane of the retina and of the elastic tissue of the arteries The eye changes cause angioid streaks due to defects in Bruch s membrane The skin lesions consist of yellow papules and plaques particularly around the neck tending to have a linear arrangement Histologically there is a patchy increase of elastic tissue with fragmentation and clumping in the deeper parts of the dermis This degenerate elastin stains with basophilic dyes The collagen is normal The histological picture resembles senile elastosis but the latter is more diffuse and the collagen is also degenerate On clinical grounds the conditions are not likely to be confused

Cutis hyperelastica (Ehlers Danlos syndrome) —This is a congenital abnormality in which there are hyperelasticity of the skin hyperflexibility of the joints scarring over the elbows and knees and soft polypi which result from injury and *hæmorrhage* into the over stretchable skin Histologically the elastic tissue is increased in amount and the fibres are coarse The collagen is atrophic and disrupted *The polypi* consist of collagen fibres with a foreign body giant cell reaction The patient shows double jointedness and is able to stretch the skin excessively Grape like swellings

ulcerate Histologically there are many histiocytes and an infiltrate in which eosinophil cells preponderate

Xanthelasma palpebrarum —In this condition there are flat or slightly raised deposi tions of cholesterol in the skin of the eyelids secondary to degenerative changes in the tissues The blood cholesterol may be normal or raised Sometimes there is diabetes but more often this is not so Under local anæsthesia the lesions can be destroyed with the cautery or the skin can be excised and left to heal without stitching

Juvenile xanthoma (nævo xantho endothelioma) presents as one or several yellow ish obtuse nodules on the limbs or on the neck and trunk of infants in the first year or two after birth The lesions regress spontaneously after a few years Histologically histiocytes containing fat (foam cells) are numerous with foreign body giant cells and there is proliferation of the vascular endothelium The blood cholesterol is normal

GRANULOMA ANNULARE

Granuloma annulare is a nodular non itchy eruption in the skin tending to form ringed lesions The cause is unknown Histologically there is a focal degeneration of the collagen giving it a ground glass appearance Around this area is an infiltrate of histiocytes lymphocytes and fibroblasts There is a deposition of mucin between the collagenous bundles The elastic tissue is degenerate A few epithelioid cells and foreign body giant cells may be present Children and young adults are mostly affected The mildest cases occur on the knuckles elbows or feet as skin coloured painless and non itchy nodules without epidermal changes Soon the nodule takes on a ringed shape or may extend in one direction and resolve in another so causing crescentic lesions A few patients have extensive and numerous lesions on the shoul ders buttocks and elsewhere as well as at the more usual sites

The lesions tend to continue indefinitely or may disappear without scarring at one site only to break out elsewhere They are however not known to be of any systemic importance and are consistent with good general health

Diagnosis is from periarteritis nodosa annular sarcoid tinea circinata and necro biosis lipoidica (*q v*) Nodules of the first named are painful The second is usually erythematous and not characteristically situated on the knuckles The third is an epidermal ringed eruption with scaling

Granuloma annulare tends to disappear after minor trauma has been applied Adhesive dressings carbon dioxide snow or slush applications or biopsy may all have this effect Treatment is unnecessary except on cosmetic grounds There is no effective systemic treatment

ERYTHEMA ELEVATUM DIUTINUM

Erythema elevatum diutinum occurs as the Bury type or as the Hutchinson type The Bury type is a firm raised dusky disc or ring of erythema It may represent the end stage of granuloma annulare The Hutchinson type consists of many firm nodules in a dusky background scattered widely over the trunk and limbs The lesions urticate on friction heat or excitement They persist indefinitely and end up as fibrous nodules The cause of the Bury type is unknown The Hutchinson type may arise from the persistent effects of an urticariogenic antigen leading to a refractory phase of the vessels so that damage occurs to the vessel walls Histologically in the Bury type there is a dense dermal mainly neutrophilic infiltrate especially around the vessels Sometimes eosinophils predominate (one form of eosinophilic granu loma) In the Hutchinson form a hyaline degeneration of the reticular fibrils around the vessels may be seen (toxic hyaline) Later fibrosis replaces the inflammatory process

Both conditions are chronic but the Hutchinson type is of more serious import because of the distressing itching and smarting

sweat duct ostia The lesions are grey or brown, warty elevations which spread peripherally, leaving a depressed, scaly, atrophic centre Treatment is by cautery destruction

Warty hard or epidermal nævi usually present as linear bands of itchy, brown warty cracked and bleeding skin The condition is unilateral, affecting the whole or part of a limb one side of the vulva, or the side of the neck or trunk (ichthyosis hystrix, nævus unius lateralis *linear nævus*) *Histologically there is* hyperkeratosis and papillomatosis but nævus cells are not present in the dermis Warty nævi are present at birth or develop at any time up to puberty and persist indefinitely Epithelioma may become superimposed Treatment is by protective dressings but if the lesion itches badly and tends to become excoriated and infected it is best excised and the area grafted

Lichenification is hypertrophy of the stratum mucosum (see Lichen Simplex)

Cutis laxa is an hypertrophy of the skin and subcutaneous tissue with lax attachment to the deeper structures with the result that the skin hangs in folds One variety is cutis verticis gyrata, a cerebriform folding of the scalp, sometimes congenital sometimes seen in acromegaly

DEGENERATIVE CONDITIONS

XANTHOMATOSES

Xanthoma tuberosum—This is a familial hypercholesteræmic xanthomatosis in which yellow nodules develop on the extensor surfaces of the elbows and knees the buttocks and elsewhere In the folds of the palms and soles there may be yellow streaks (xanthoma planum) Internal organs are also affected particularly mucous surfaces the tendons the endocardium and the intima of blood vessels Numerous xanthoma (foam) cells are seen in the dermis These are phagocytes containing lipoid material The cutaneous lesions are of no importance in themselves but the associated vascular lesions may cause death through coronary occlusion

The patient should be put on a diet with a small fat, vitamins A and D content By this means after several months the skin lesions may become smaller The aim of the treatment is to bring about a similar regression in the vascular lesions Lesions identical to those of xanthoma tuberosum also occur with *biliary cirrhosis* but in this condition the lesions are preceded by jaundice for months or years

Secondary xanthomatosis consists of yellowish red transitory, itchy papules, which consist of foam cells with an inflammatory reaction The condition is brought about by hypercholesteræmia and occurs in primary xanthomatosis diabetes mellitus (xanthoma diabeticorum) and biliary cirrhosis also in hypercholesteræmia sine xanthoma tuberosum Treatment is of the primary condition

Cholesterol histiocytoses are normocholesteræmic conditions reticuloses with secondary cholesterol depositions Letterer Siwe s disease is the infantile form in which petechiæ papules and pustules are observed and in which fever anæmia liver spleen and lymph node enlargement occur with multiple bony defects The condition is fatal before lipoid deposits develop in the skin

In the Hand Schuller Christian disease there may be diabetes insipidus exophthalmos dwarfism, enlargement of liver spleen and lymph nodes and bony defects The skin condition consists of yellowish macules and nodules with greasy overlying scales giving a resemblance to a mild infective dermatitis It tends to affect the scalp face and the flexures Petechiæ may also be present Histologically there are numerous histiocytes and some foam cells

Eosinophilic granuloma—This is a localised form of the same syndrome affecting chiefly the bones Sometimes the skin is affected with granulomata which tend to

GOUT

Gout —In this disorder of purine metabolism white nodules due to deposits of urates (tophi) are found in the cartilage of the ears and in the subcutaneous tissues around joints particularly the metacarpophalangeal joints of the great toes

MYXŒDEMA

Myxœdema —In generalised myxœdema the skin is dry pale and thickened In circumscribed (cutaneous) myxœdema which occasionally develops after operations on the thyroid or with thyroid adenomata firm raised dome shaped waxy skin coloured or yellowish nodules and plaques form mostly on the anterior aspects of the legs sometimes also on the face or arms Histologically the lesions contain a large amount of mucin Treatment is ineffective

EPIDERMAL TUMOURS

BASAL CELL PAPILLOMA (SENILE OR SEBORRHŒIC WART)

Basal cell papillomata are light to dark brown roughly papillated excrescences with non infiltrated bases and a greasy candle wax texture They occur with increasing frequency after the age of 40 and affect especially the scalp the face and the trunk They can easily be scraped off exposing a raw fleshy base

Ætiology and Pathology —Their cause is unknown They are believed by some to be infective by others to be a late nævoid condition

Histologically there are small epithelial cysts due to invagination of the epidermis There is also acanthosis with prolonged rete ridges The dermis shows little inflammatory reaction

Course and Prognosis —These lesions are benign but they may become secondarily infected

Treatment —For small superficial lesions brief (1 second) applications of carbon dioxide snow are effective Larger lesions are best dealt with by curettage and cautery under local anæsthesia

SQUAMOUS CELL PAPILLOMA (JUVENILE OR INFECTIVE WART VERRUCA)

Ætiology and Pathology —Warts are infective epidermal tumours caused by a virus They are auto inoculable and may appear in linear form in scratch marks They are commonest in childhood and young adults though elderly persons may be affected

Histologically there is focal acanthosis and gross hyperkeratosis with a variable degree of inflammatory infiltrate in the dermis The epidermo dermal junction is intact with no evidence of invasion of the dermis Mitoses may be numerous

Clinical Picture —Warts are described on a morphological basis as plane acuminate filiform digitate etc and from their situation as genital plantar etc On the scalp they tend to be digitate in the beard area filiform on the faces of children plane on the hands and knees grey brown circular excrescences (common warts verrucæ vulgaris) except around or under the nails where they may resemble hangnails or corns with considerable discomfort On the genitalia warts are usually acuminate (condylomata acuminata) and on the soles of the feet they are painful inverted embedded in hyperkeratosis and perhaps confluent in a mosaic pattern

Course and Prognosis —This is extremely variable Warts may disappear

Treatment is symptomatic and largely ineffective In the Bury form carbon dioxide snow is worth a trial In the Hutchinson form, antihistamine drugs may reduce the itching and urtication

NECROBIOSIS LIPOIDICA

Necrobiosis lipoidica is a condition in which lipoid deposition occurs in areas of degenerate or necrobiotic collagen Diabetes mellitus is often present or may subsequently develop Ill defined areas of poorly staining somewhat basophilic collagen are present in the dermis The collagen bundles are disorderly and disrupted In and around the area is an infiltrate of lymphocytes, histiocytes and fibroblasts A few epithelioid and foreign body giant cells may be seen and sometimes foam cells The blood vessels show fibrosis and endothelial proliferation, often with thromboses Stains for fat show much extracellular lipoid material

The lesions usually appear on one or both shins but are occasionally seen at the ankles on the feet or hands or elsewhere They consist of slightly depressed plaques of shiny atrophic, waxy yellow skin, with well defined margins and dilated venules showing clearly The centre may ulcerate On the hands the appearance differs the lesion resembling granuloma annulare

The malady often becomes inactive after a time but it never regresses Diagnosis is from other atrophic conditions and from granuloma annulare In the latter the histological changes are very similar but more focal and vascular changes are not visible Mucin deposits are found but no lipoid as in necrobiosis There is no effective treatment

AMYLOIDOSIS

Amyloidosis can affect the skin in three ways primary systemic amyloidosis, primary cutaneous amyloidosis (lichen amyloidosis) secondary systemic amyloidosis

Primary systemic amyloidosis affects the skin particularly of the face with non itchy waxy yellowish semi translucent nodules and plaques Petechiæ may be present In addition there is extensive involvement of voluntary and involuntary musculature, the cardiovascular system and the gastro intestinal and genito urinary tracts Macroglossia occurs There may be multiple myelomata and Bence Jones proteinuria Radiographic examination of the bones and sternal biposy are helpful in diagnosis

Amorphous deposits of amyloid are scattered throughout the dermis In secondary systemic amyloidosis the skin is very rarely affected In primary cutaneous amyloidosis the lesions usually occur on the legs as very itchy lichen planus like nodules—conical brownish or violaceous verrucose lesions which may coalesce to form large plaques Deposits of amyloid are present in the upper dermis There is no effective treatment

CALCINOSIS

Calcinosis cutis may be the result of hypercalcæmia due to hyperparathyroidism excessive vitamin D (calciferol) therapy chronic kidney disease or gross destruction of bone as in osteomyelitis or malignancy The skin is rarely affected most deposits occurring in the kidneys lungs or stomach Far commoner is normocalcæmic calcinosis cutis secondary to some degenerative process in the skin hypoderm muscles or tendons Scleroderma or dermatomyositis are often present but sometimes no cause can be found The depositions mostly take place in the fingers wrists elbows and feet and can be felt as hard masses bulging the skin often white and sometimes ulcerating Treatment is of the primary condition when this is possible

Clinical Picture—Pearly yellow pink or skin coloured umbilicated nodules occur singly or in groups They may occur anywhere on the skin and transference may take place from the breast of a mother to the face of her suckling or in the ano genital region during coitus Secondary infection may cause a lesion to become grossly enlarged ulcerated and purulent or necrotic

Diagnosis from warts is simple if inspection is made with a hand lens

Treatment—A phenolised probe or pointed orange stick is forced into each lesion or the tumours can be curetted off Antibiotics are ineffective as a rule but one or two successes have been claimed

EPIDERMAL CYSTS (WENS)

Milia are pinhead sized white cysts in the epidermis They are usually multiple and are found with acne or on apparently normal skin on the face they may also develop over some pathological condition such as epidermolysis bullosa or pemphigoid

Large epidermal cysts are often found on the scalp behind the lobes of the ears on the face scrotum and elsewhere A few of them are sebaceous cysts which vary in size from a pinhead to a walnut and show a dimple representing the follicular opening

Ætiology and Pathology—Epidermal cysts are possibly derived from the lanugo hair follicles and consist of a whorl of epithelial cells Sebaceous cysts are believed to be nævoid They may occur in large groups in steatocystoma multiplex The cysts are lined with squamous epithelium and contain horny and sebaceous material

Diagnosis is from dermoid cyst lipomata and cystic acne (*q v*)

Treatment—The cyst is incised and its odourless contents are expressed In epidermal cyst this is sufficient but in sebaceous cyst the offensive cheesy contents are first expressed and then the capsule is pulled out with artery forceps If secondary infection has occurred it is only possible to incise the cyst and removal of the capsule has to be deferred until inflammation has subsided

DERMOID CYST

These rare tumours occur in the mid line of the body or at the outer end of the brow They are skin coloured and not dimpled The cyst is lined with keratinising cells and may contain rudimentary sweat glands and pilosebaceous follicles as well as layers of keratin sebaceous material and sometimes hair cartilage or bone

Treatment is by removal if desired

IMPLANTATION CYST

These occur in the skin or more often in mucous surfaces following an injury which carries epidermal cells through a break in the surface

Treatment is by excision

BASAL CELL CARCINOMA (RODENT ULCER)

Ætiology and Pathology—The cause of these tumours is unknown They usually occur in the fifth sixth or seventh decades but occasionally appear in early adult life The majority arise in the area enclosed by two lines drawn from the tip of the ear to the eyebrows and from the lobe of the ear to the mouth but no area of the skin is immune except the palms and soles rodent ulcers may develop on the scalp the chest or abdomen or on the limbs Apparent precipitating causes include sunlight heat mechanical trauma and the ingestion of inorganic arsenic

Histologically there is a proliferation of basal cells without evidence of invasion

without treatment or they may spread They are amenable to suggestion in a proportion of cases They may recur even after the most careful curettage

Diagnosis may have to be made from one or other of keratosis corn callus, molluscum contagiosum, molluscum sebaceum squamous carcinoma papillary mole or nævus subungual exostosis acanthosis nigricans condyloma latum, verrucose lichen planus and lupus verrucosus (q v) Histological examination is sometimes necessary

Treatment —A waiting policy is sometimes justifiable because a proportion of warts disappear spontaneously On the scalp and beard area a combination of curettage and cautery is best Plane warts on the face or hands may be dealt with by daily applications of 1 per cent brilliant green in collodion salicylic acid fractional X ray exposures are sometimes used but simple suggestion may prove just as effective

On the hands if suggestion and local keratolytics and caustics fail recourse may be had to curettage and cautery under local anæsthesia or to carbon dioxide snow applications 30 to 90 seconds on each occasion depending on the size and situation of the lesions at intervals of 2 to 3 weeks Carbon dioxide snow is especially useful for paronychial and subungual warts because it causes less deformity than curettage and cautery

On the genitalia podophyllin 20 per cent in liquid paraffin is the treatment of choice The application is made on gauze to the penis or vulva It is applied at bedtime and removed on rising the affected area being cleaned with liquid paraffin A similar application is made the next night but after this at least a week should elapse before any further treatment of this sort is given Podophyllin causes a brisk inflammatory reaction after which all or most of the warts are shed A second course of treatment a week later may dispose of the remnants Sometimes this treatment fails to relieve extensive vulvar warts and then curettage and cautery under general næsthesia may be necessary

Plantar warts may occasionally disappear spontaneously but usually it is necessary to treat them either by caustics podophyllin 25 per cent formalin 10 per cent or by carbon dioxide snow applications 30 to 90 seconds at each treatment X ray treatment is contraindicated it succeeds in only about 60 per cent of cases a success rate equalled by many simpler measures and far exceeded by curettage and cautery Further, if X ray treatment fails the tissue is left to some degree devitalised repeated X ray treatment can cause sloughing of the deeper tissues with much suffering and deformity and perhaps necessitating grafting

Curettage and cautery offers something above 90 per cent prospect of success The injection of the local anæsthetic is a difficult part of the procedure For this purpo e the patient lies prone on the operating table, this provides flexion of the foot and relaxation of the plantar fascia and also directs a timid patient s attention away from the field of operation The injection is made slowly if possible through thin skin at the side of the foot After thorough curettage the horny collarette is trimmed away and the whole area is cauterised

MOLLUSCUM CONTAGIOSUM

A virus infection of the skin characterised by globular slightly umbilicated nodules

Ætiology and Pathology —The condition is acquired by direct contact, non venereal or venereal

Histologically there is a symmetrical proliferation of the epidermis in oval or pear shaped lobules with degeneration of the epidermal cells caused by large cytoplasmic inclusion bodies homogeneous and eosinophilic which push the nuclei aside (molluscum bodies) The granular layer is thickened and a mass of horny material forms the central area of the tumour

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Histologically there is a proliferation of basal cells without evidence of invasion

Globular clumps of darkly staining basal cells are seen The cells may remain undifferentiated or may show differentiation towards horny or glandular structure (keratotic adenoid and cystic rodent ulcers) The cellular mass expands horizontally and vertically If expansion is mostly horizontal (superficial rodent ulcer) the tendency to ulceration is less marked if it expands vertically the mass finally reaches a size in which the nutrition of its more centrally and superficially placed cells is inadequate and ulceration results

Clinical Picture —The appearance of rodent ulcers is extremely variable depending on the situation superficiality or depth and presence or absence of ulceration or infection Types include (1) the button like nodule (2) the pigmented nodule, (3) the rodent ulcer (4) the superficial type (5) the cicatricial type (6) the morphœa like scalp lesion (7) the cystic type Rodent ulcers may be multiple

The most common form is a pearly nodule which expands to form a button like tumour with small vessels coursing over its surface Sometimes the nodule is more globular and cherry like It may be skin coloured, grey or brown The rodent ulcer may bore deeply from the earliest stages (ulcus terebrans) or a nodule may only start to ulcerate after attaining a certain size, 1 cm in diameter or more In the first form there is a slightly raised rolled edge to the ulcerated area In the latter, the ulceration is at first a relatively inconspicuous feature in the centre of the nodule and gradually extends

The superficial basal cell carcinoma may be multiple It usually occurs on the trunk and often there is a history of prolonged medication with Fowler s solution It has a rolled edge so slightly elevated that it is not always easy to recognise it except with the aid of a hand lens The lesion resembles psoriasis, being a circumscribed irregularly red oval patch of abnormal scaling perhaps with some serous crusting in places The cicatricial basal cell carcinoma is also usually superficial but leaves a scarred and somewhat atrophic skin in the area behind its extending edge On the upper forehead and scalp basal cell carcinomata tend to develop horizontally and resemble morphœa (card like basal cell carcinoma) Rarely rodent ulcers a e clinically cystic This type tends to be dome shaped with a shelving edge and there may be considerable pigmentation

Course and Prognosis —The course varies according to the situation depth and amount of differentiation The superficial type may slowly extend parallel with the surface for many years The ulcus terebrans erodes early and deeply with the result that in a year or two important subcutaneous structures may be destroyed In these cases death may occur from hæmorrhage or secondary infection Metastases from basal cell carcinomata are very rare

Diagnosis —Rodent ulcers must be differentiated from granulomatous and reticulotic conditions from Bowen s disease and from psoriasis The long duration and hard pearly edge sometimes somewhat serpiginous usually makes the diagnosis easy Syphilitic ulcers are of short duration in relation to their size In some cases the diagnosis is not possible on clinical grounds and reliance has to be placed on biopsy and histological examination This also applies to the differentiation between recurrences of rodent ulcers and radiation necrosis or ulceration

Treatment —This consists of surgery with plastic repair when nece ary X irradiation or radium or in a few superficial examples destruction by carbon dioxide snow Surgery to be effective must include an area of apparently normal skin all round the lesion at least 0 75 cm wide This may be easy in some places impossible or too disfiguring in others Surgery is a necessity in dealing with recurrences where further X irradiation is thought to be inadvisable it may entail extensive plastic repair

X irradiation is best for lesions in situations which render excision difficult The total dosage used by radiotherapists varies A total of 3600 r, fractionated so as to give 720 r daily for 5 days, gives a better cosmetic result than 3600 r at one

treatment Some prefer a total dosage of 4500 r claiming that recurrences are less likely but it is probable that more recurrences are due to insufficient coverage of the apparently normal zone around the lesion than to insufficient dosage Basal cell carcinomata spread along the lymphatics beyond the visible edge and it is this clinic ally imperceptible spread that leads to recurrence unless a zone 0 75 cm to 1 cm wide is irradiated as well as the visible tumour

Radium is sometimes more useful than X rays and can be used as moulded surface applications or as needles or seeds of radon

Carbon dioxide snow is sometimes used for superficial rodent ulcers on the trunk applications of 90 seconds duration are made under firm pressure The resultant reaction has to be treated like a burn

SQUAMOUS CELL CARCINOMA

A tumour which is more rapidly growing than the basal cell carcinoma and which may give rise to metastases

Ætiology and Pathology —Squamous cell carcinomata are of varying grades of malignancy Some tend to form horn and are of low malignancy in others the cells remain undifferentiated and the lesions are more malign

Clinical Picture —The lesions are firm and nodular with shelving edges and rapidly ulcerate or form cauliflower like growths There is no rolled edge The sites most often affected include the face lower lip ear and the backs of the hands Squamous carcinomata are usually preceded by one or other of the precancerous conditions mentioned in the next section They rarely arise on apparently healthy skin usually the preceding pathological condition is brought about by excessive and prolonged solar irradiation by past X ray treatment or by some other physical irritant Glandular metastases occur early particularly from the ear lip or hand

Course and Prognosis —The lesion extends at first within the dermis and then invades the hypoderm At this stage spread by the lymphatics to the lymph nodes is more likely These lesions are as a result much more likely to be fatal than are basal cell carcinomata

Treatment is by excision or X irradiation On the lip and ear wedge excision offers the best prospects At other sites too surgery is preferable to X rays because the cells may be relatively radio insensitive Sometimes a combination of excision and irradiation is used Block dissection of the lymph nodes draining the area may be necessary Biopsy may be performed on skin sites if it is considered necessary but on the vermilion surface of the lip it is inadvisable Here V excision should be done and histological study made of the excised material

SECONDARY CARCINOMA OF THE SKIN

This occurs by lymphatic spread from a breast cancer or as cutaneous metastases usually from the breast (rarely from stomach uterus lungs prostate or ovary)

In the first form there is a hard red but pitting area of skin with a well marked border (carcinoma erysipelatoides cancer en cuirasse) It usually occurs in the axillæ or on the chest perhaps following a radical mastectomy

The metastatic form occurs as one or several firm white nodules in the skin the nature of which may be suspected or only discovered by biopsy

Treatment is symptomatic because the primary lesion may still be present or other inaccessible secondaries may exist

PRE MALIGNANT AND BORDER LINE CONDITIONS

Kerato acanthoma (molluscum sebaceum) is a benign neoplasm of the skin which though histologically resembling a squamous and horny carcinoma has a self limited

natural history ending in spontaneous resolution at about 3 months Its histological structure is that of a symmetrical and molluscoid squamous horny carcinoma.

Tar warts are possibly a variety of kerato acanthoma but are more uncertain in their course, some being shed while others go on to carcinoma Kerato-acanthoma sometimes arises on normal skin whereas squamous carcinomata arise at sites of keratoses and other epidermal abnormalities The lesion is button shaped with almost vertical edges whereas in squamous carcinoma the edge is shelving In the centre of the button is a horny plug Ulceration does not occur If nothing is done the nodule shrinks up and disappears, leaving an irregular crater with thickened lips of epidermis

Treatment —Thorough curettage of the lesion usually gives a better cosmetic result than X-ray treatment or waiting for spontaneous clearance If doubt exists as to the diagnosis the lesion should be treated as for squamous carcinoma either by wide excision or by adequate X-irradiation

BOWEN'S DISEASE

This precancerous condition may occur on the face, body or limbs

Pathology —There is an irregular acanthosis and large cells with dark nuclei and vacuolation of the cytoplasm are scattered through the epidermis They are similar to the cells seen in Paget s disease of the nipple

Clinical Picture —The lesions are usually itchy, pink and brown scaly or papular patches, sometimes slightly exudative with well marked but not rolled edges

Course and Prognosis —If untreated a termination in squamous carcinoma is likely after an interval of months or years

Diagnosis from superficial rodent ulcer is by the absence of a rolled edge from psoriasis by the absence of lesions elsewhere the chronicity of the lesion at one site the itching and the absence of typical psoriatic scales From mildly infected eczematous dermatitis the differential diagnosis may be impossible on clinical grounds alone and biopsy is then advisable

Treatment is by carbon dioxide snow, a firm application lasting 90 seconds This causes an inflammatory reaction sloughing of the affected area and replacement of the pathological skin by a smooth scar X ray treatment may also be used in doses equal to or greater than those used for skin cancers Sometimes excision is more suitable

PAGET S DISEASE

A pathological condition of the nipple and its ducts occurring with or soon followed by carcinoma of the nipple ducts

Pathology —There is parakeratosis with irregular acanthosis and clear 'Paget cells' scattered in the stratum mucosum

Clinical Picture —There is scaling and pinkness of the skin around one of the nipples, with slight palpable thickening The nipple may be in part or totally, destroyed in the process or it may be retracted It is clearly smaller than the other nipple Lymph nodes are not usually palpable in the axillæ and no abnormality can be felt in the breast.

Course and Prognosis —Carcinoma of the duct coexists with Paget s disease or soon follows it The malady if untreated, leads to metastatic carcinomatosis

Diagnosis is from eczema of the nipple This may be secondary to scabies, or in adolescents and young women it may be a manifestation of the asthma prurigo syndrome or of neurodermatitis In either of these conditions infiltration of the lesions is absent and the nipple is intact and equal in size to the other nipple Eczema of the breast may also develop from maceration by milk and the use of rubber dress protectors by lactating women

Treatment is by mastectomy Lymph node dissection is usually unnecessary X irradiation is contraindicated

QUEYRAT S ERYTHROPLASIA

This is a rare condition similar to Bowen s disease but affecting the glans penis *or the vulva*

Clinical Picture —There is a clear cut shiny pink slightly infiltrated and elevated patch

Diagnosis is from psoriasis and chemical balanitis In doubtful cases biopsy is indispensable

Treatment is by X irradiation

ACANTHOSIS NIGRICANS

This occurs in a juvenile benign form and in an adult malignant form

Ætiology and Pathology —The juvenile form is of unknown ætiology possibly nævoid The adult form is nearly always associated with a carcinoma usually of the stomach

The histology of both types is the same and consists of marked hyperkeratosis and papillomatosis with an irregular acanthosis and hyperpigmentation in the melano blasts and melanophores

Clinical Picture —The skin of the flexures is darkened thickened and lies in velvety folds In severe cases of the adult form the lips gums tongue and œsophagus may also be affected Clinical examination may reveal evidence of a new growth but sometimes the most careful search gives negative results yet at post mortem a neoplasm is discovered

Course and Prognosis —The juvenile form is benign but the adult form nearly always ends in death from the associated visceral neoplasm

Diagnosis is from warty nævi which are usually unilateral and linear and not confined to the flexures Darier s disease has a somewhat similar distribution but is usually more widespread the individual lesions are harder and the histology is distinctive

Treatment —Laparotomy is justifiable even if a visceral neoplasm cannot be located by clinical methods

KERATOSIS SENILIS VEL SOLARIS

This occurs mostly on the exposed surfaces of the skin except the form that may develop after inorganic arsenic medication which occurs more on the trunk than on the exposed parts

Ætiology and Pathology —Damage to the skin by excessive solar or X irradiation or by the ingestion of arsenic is the chief factor Age is of secondary importance, the lesions occurring in children with xeroderma pigmentosa in relatively young persons who have been much exposed to the tropical sun but rarely occurring even in extreme old age unless there has been considerable exposure to the sun throughout life

Histologically there is hyperkeratosis and parakeratosis Acanthosis precedes a frank prickle cell carcinomatous proliferation

Clinical Picture —Ill defined or clear cut dirty grey hard rough and scaly areas of skin are seen on the face or on the backs of the hands

Course and Prognosis —At any time keratoses may take on malignant proper ties on the other hand they may continue for years without this change occurring

Diagnosis *is from seborrhœic warts Keratoses are hard* rough and dirty grey

in colour, while seborrhœic warts are soft or firm, of candle wax texture and with a shiny brown surface which is often papillated

Treatment is by freezing with carbon dioxide snow for 15 to 30 seconds, provided there is no infiltration of the base Once the base has become infiltrated, the lesion should be treated as a squamous carcinoma (*q v*) with or without preliminary biopsy

CUTANEOUS HORN

This is a keratosis in which horn formation is carried out to excess

Clinical Picture —A horn grows either from an area of squamous papillomatous change or from an area of squamous carcinomatous change In the former the base is not infiltrated in the latter it is hard and elevated

Treatment depends on the changes taking place in the base If they are simply papillomatous curettage of the lesion through its base and cautery are usually sufficient If there is a suspected carcinomatous base the lesion should be widely excised or dealt with by radiotherapy with or without a preliminary biopsy

LEUCOPLAKIA

This is keratosis of a mucous surface and like keratosis on the skin it may remain innocent or develop into carcinoma (see Diseases of the Lips and Mouth)

NÆVOID AND ORGANOID EPIDERMAL TUMOURS

These are tumours either present at birth or first appearing later in life but running a benign course

NÆVUS SEBACEUS (JADASSOHN)

This is a yellow slightly raised firm nodule with a papillated surface usually occurring on the scalp or face and present at birth

Pathology shows mature sebaceous glands

Course and Prognosis —At or after puberty a basal cell carcinoma may develop on a nævus sebaceus Apart from this the lesion remains static through life except for any secondary infection that may occur from trauma by a comb or some other means

Treatment is by excision if desired Cautery or diathermy are unlikely to be effective For carcinomatous changes excision possibly with grafting or radiotherapy is necessary

SENILE SEBACEOUS *NÆVUS*

This is probably a delayed nævus Like the nævus sebaceus it consists of mature sebaceous glands It occurs on the forehead or face of persons of 50 or over as yellowish somewhat translucent nodules No treatment is necessary but the cautery can be used to destroy it

ADENOMA SEBACEUM (PRINGLE)

This is not an adenoma but a sebaceous nævus with hyperplasia of blood vessels and connective tissue The lesions occur on the part of the face near the nose as yellow brown or purplish nodules with telangiectasia The condition is associated with epilepsy mental deficiency *nodular sclerosis* of the brain and tumours of the kidneys heart and other organs (epiloia) The brain and retinal tumours are glio

mata those of the heart rhabdomyomata and those of the kidneys angiomata fibromata adenomata or mixed tumours No treatment is necessary for the skin condition but the nodules can be destroyed with the galvanocautery

FORDYCE CONDITION

This consists of ectopic sebaceous glands in the mucous surfaces of the lips or of the cheeks The lesions are yellow pinhead or larger soft nodules the histology of which is of a sebaceous glandular nature No treatment is necessary Reassurance may be necessary that the lesions are not luetic tuberculous cancerous or lichen planus The condition is so common as to be regarded as physiological

SYRINGOCYSTADENOMA PAPILLIFERUM

This occurs as a skin coloured or yellowish papilliferous lesion with crusting on the scalp It is an adenoma of apocrine ducts It may occur together with sebaceous nævus and like the latter may be complicated by basal cell carcinoma Treatment is preferably by excision Destruction by galvano cautery is likely to be followed by a recurrence

HYDRADENOMA PAPILLIFERUM

This occurs on the labia majora and perineum as a solitary skin coloured nodule of split pea size or smaller Malignancy does not develop The condition is an adenoma of apocrine glands

APOCRINE EPITHELIOMATA

These are of two varieties in syringoma differentiation of the cells is towards apocrine duct cells in cylindroma differentiation of the cells is towards apocrine gland cells

Syringomata occur mostly in women as multiple skin coloured or yellowish soft nodules of pinhead size and larger on and around the eyelids on the chest and abdomen and sometimes elsewhere No treatment is necessary but for cosmetic reasons they may be treated with carbon dioxide snow or the galvano cautery

Cylindromata (turban tumours) occur as rounded smooth elevations on the scalp and sometimes on the face and upper trunk beginning in young adults and slowly enlarging up to the size of grapes sometimes giving the scalp a cerebral appearance Treatment is ineffective because the extent of the lesions makes surgery impracticable and radiotherapy is of no use

TRICHO EPITHELIOMATA (EPITHELIOMA ADENOIDES CYSTICUM) (BROOKE S DISEASE)

These occur as multiple skin coloured nodules resembling basal cell carcinomata developing in early adult life on the scalp and face It is a familial disorder The tumours contain numerous horn cysts and rudimentary hair Some areas may closely resemble basal cell carcinoma and occasionally after many years these tumours take on the properties of rodent ulcers

Treatment —The tumours are usually too numerous for surgery and they are radio insensitive Active treatment is therefore best deferred unless malignancy develops in any one nodule when either radiotherapy or surgery is necessary

CALCIFYING EPITHELIOMA (MALHERBE)

This is a rare solitary movable, sharply demarcated often encapsulated tumour situated in the lower dermis Histologically there are basal cells adjoining pale "ghost cells with a foreign body giant cell reaction nearby Diagnosis is made histologically from a calcified sebaceous cyst, which has squamous cells adjoining the cyst cavity Treatment is by excision

CHONDRODERMATITIS NODULARIS CHRONICA HELICIS

This condition presents clinically as a painful nodule on the helix It is best considered here although it is uncertain whether it is inflammatory or neoplastic It usually occurs in men it may be bilateral and it interferes with sleep by causing discomfort when the head rests on the pillow

Pathology —There is diffuse inflammation in the corium It has been suggested that it is a form of glomus tumour

Treatment is by wedge excision including a portion of cartilage Anything less leads to recurrence

TUMOURS OF THE DERMIS

MOLES

A mole (pigmented fleshy, sometimes hairy nævus) is an elevated light or dark brown firm fleshy nodule occurring singly or scattered over the face A papillated form also occurs

Pathology —There are orderly circumscribed clusters of nævus cells in the dermis separated from the epidermo dermal junction and showing no mitotic activity Mixed dermal and epidermo dermal junctional nævi also occur in which the active junctional component is potentially malignant

Course and Prognosis —Moles tend to enlarge as age advances and they also get more hairy Folliculitis may develop and cause tenderness and swelling but malignant degeneration rarely, if ever occurs

Treatment is unnecessary except as a cosmetic matter The hairs may be removed permanently by diathermy or electrolysis and this is often sufficient Excision may be performed but destructive procedures of cautery carbon dioxide snow or diathermy are inadvisable they may result in ugly scarring and cause incomplete removal Operations on moles necessitate removal of the dermis in full depth

LENTIGO MALIGNA

This is a state of premalignant proliferation of lentigo (*q v*) in the plane parallel to the surface It is to malignant melanoma much as Bowen s disease is to squamous carcinoma The lesions appear in elderly persons as a very dark brown impalpable expansion of a lentigo There is no lymph node enlargement

Pathology —There are no nævus cells in the dermis but there is great irregularity and dropping off of the cells at the epidermodermal junction into the dermis The basal layer is markedly pigmented and there are many clear cells

Treatment is by wide excision A margin of 1 cm or less may be followed by recurrence in the scar

MALIGNANT MELANOMA

This the most malignant of all tumours arises from lentigines lentigo maligna or from mixed or junctional nævi It may also arise from the choroid

Pathology —There is extreme disorganisation of the epidermodermal junction with much mitotic activity in atypical nævus cells Beneath is a dense inflammatory infiltrate invaded by strands of the pigmented nævus cells Often the epidermis becomes permeated by tumour cells and disintegrates leading to the characteristic bleeding or ulceration of these lesions

Clinical Picture —Any mole or lentiginous macule should be regarded with great suspicion if it enlarges becomes darker bleeds scabs or becomes ulcerated or painful The classical malignant melanoma is a dark brown or bluish black soft easily bleeding nodule If it arises from a lentigo maligna there is a flat surrounding impalpable dark zone of a somewhat lighter tint than the melanoma itself Regional lymph nodes may be palpably enlarged or there may be extensive lymphadenopathy beyond the reach of the diagnostician s finger for example in the iliac chain Some melanomata are light brown and a few are skin coloured (amelanotic) and perhaps difficult to recognise even on histological grounds from anaplastic carcinoma

Course and Prognosis of melanomata is grave in the extreme Even if removed at the first recognition metastases are only too often found already to have occurred Once a melanoma has taken on malignant proliferation therefore the prognosis should be guarded there may be no recurrence after operation or metastases may declare themselves after a technically perfect operation Metastasis may take place in the lymph nodes in the liver or lungs or in the brain giving rise to symptoms of a cerebral tumour sometimes long after the primary lesion has been removed

Treatment —Without performing a biopsy a suspected melanoma should be very widely and deeply excised On no account should the lesion be manipulated by forceps in the process of removal Sometimes for example with Hutchinson s melanotic whitlow amputation is a better plan More drastic block dissections of the regional lymph nodes are sometimes carried out Melanomata are non responsive to X ray treatment but X rays are sometimes used before excision to check mitotic activity during the time of removal

BLUE NÆVUS (MONGOLIAN SPOT)

This is a button like firm slaty blue nodule usually found in the sacral region

Pathology —Deep in the dermis are spindle shaped cells containing melanin and lying with their long axes parallel to the surface The epidermis is normal but with the upper dermis it acts as a light filter and so gives the nævus its bluish tint

Course and Prognosis —The lesion is benign and static No treatment is necessary but excision can be carried out if the patient wishes it

KELOID

A keloid is a pink or white firm raised tumour often with claw like extensions beyond the limits of the original scar Histologically there is fibroblastic proliferation in the early stage and dense fibrosis in the later stages Keloids may form for no obvious reason or at sites of ingrowing hairs acne wounds tattoo marks vaccination scars or burns Predisposition both racial and personal is marked the coloured races being most affected and some white persons more than others

Acne keloidalis nuchæ is probably a keloid due to ingrowing hairs True acne keloids occur on the face and trunk

Treatment —Repeated fortnightly carbon dioxide snow applications 10 to 30 seconds on each occasion may flatten the lesions or excision followed by radiotherapy to the scar may prove effective Excision alone is usually most disappointing recur rence taking place

FIBROMA DURUM (SCLEROSING HÆMANGIOMA DERMATO FIBROMA, HISTIOCYTOMA, FIBROMA EN PASTILLE)

These deeply situated, firm globular tumours occur in the skin of the legs more than anywhere else *They may be single or multiple* *The colour* may be pink, light brown, bluish or skin coloured depending on the amount of vascularisation, lipoid or hæmosiderin deposition or fibrous tissue They are usually painless

Pathology —*The histological appearance* varies with the degree of maturity Early tumours contain a preponderance of histiocytes and endothelial cells, older tumours contain fibroblasts and fibrous tissue Infantile xanthomata the yellow *nodules known as nævo xantho endothelioma* are histiocytomata

Treatment —Histiocytomata do not recur after excision

FIBROMA MOLLE (FIBROMA COLLI OR SKIN TAGS)

Fibroma molle is a soft, fleshy, sometimes pedunculated tumour, often found *on the necks and axillæ of middle aged women* *The histology is that of normal* connective tissue It is possible that these lesion represent a forme fruste of von Recklinghausen s disease

Treatment—Destruction or removal by means of the galvano cautery gives excellent results

DERMATO FIBROSARCOMA PROTUBERANS

This is a locally recurrent form of fibroma One or several grouped nodules *skin coloured or purple form an irregular mass which may ulcerate* There is local invasion of tissue but metastasis is unusual except after many years True metastasising fibrosarcoma is very rare on the skin

***Treatment** —Local excision should include a wide area of apparently normal* skin if recurrence is to be avoided

MYXOMATOUS DEGENERATION CYSTS (SYNOVIAL CYSTS)

These occur mostly on the fingers near the distal interphalangeal joints They *are tense translucent and globular and contain mucinous fluid* The wall of the cyst is made of fibrous tissue

COLLOID MILIUM

This is a pinhead sized, translucent yellow nodulation usually of the forehead The slimy contents are degenerate collagen and the cysts are lined with collagen

NEUROFIBROMATOSIS (VON RECKLINGHAUSEN S DISEASE)

In this malady there are numerous soft skin coloured or brownish *purple tumours*, mostly pedunculated varying in size from pinhead size to masses the size of an orange *(molluscum fibrosum)* Yellowish brown macules of varying sizes and shapes (cafe au lait spots) are also present

Pathology —Wavy nerve sheath fibrils in loose strands and whorls are inter*spersed* with reticulum fibrils and collagen Mucoid degeneration may occur The café au lait spots show an increase of melanin pigment

Clinical Picture —The fully developed clinical picture is characteristic but *formes* frustes also occur in which the diagnosis may be more difficult In addition to the skin lesions there may be nodules on the peripheral nerves and in the central nervous system in the chest or abdomen and under the periosteum

Course and Prognosis —Malignant change is rare in the skin lesions but more common in the visceral ones

KAPOSI S IDIOPATHIC HÆMORRHAGIC SARCOMA

This condition is probably a benign angiomatosis and is not sarcomatous Histologically there are spindle cells and numerous dilated blood vessels with extravasations

Clinical Picture —Brown or purple nodules develop usually on the feet sometimes on the hands or on other parts of the skin Visceral lesions are common particularly in the lungs and abdominal organs and lymph nodes The skin lesions are not tender They first appear in early or middle adult life mostly in Jews slowly enlarge and then become static or regress They may ulcerate

Course and Prognosis —The course is usually benign though occasionally sarcomatosis has been reported as a terminal feature

Treatment —Radiotherapy may diminish the size of the lesions Apart from this dusting powders to the feet and measures directed to preventing or controlling ulceration are indicated Watch must be kept for symptoms of visceral involvement

OTHER SARCOMATA

Liposarcoma myxosarcoma osteosarcoma rarely occur in the skin

LEIOMYOMA

Leiomyoma may be a solitary tumour or it may occur in groups

Clinical Picture —The tumours are split pea sized smaller in the grouped form or larger in the solitary type They are yellowish brown and very tender to the touch particularly the grouped form The grouped leiomyomata arise from the arrectores pilorum muscles and the lesions may occur on the face trunk or limbs particularly the extensor surfaces Solitary leiomyomata may arise from involuntary muscle in the skin of the breasts scrotum or labia majora or from vascular musculature (angiomyomata)

Treatment —The only effective treatment is excision

LIPOMATA

These are soft freely movable often ill defined tumours in the subcutaneous tissue They may be single and massive for example in the neck or multiple The latter variety may be painful (Dercum s disease)

Treatment is by excision when necessary

HÆMANGIOMATA

NÆVUS FLAMMEUS (PORT WINE STAIN)

This is a hæmangioma of statically dilated vessels present at birth and often persisting through life although some small lesions on the eyelids and face may disappear after a few weeks of extra uterine life

An hæmangioma at the nucha is very common (Unna s nævus physiological nævus) Other sites commonly affected are the mid line of the forehead and one half of the face or even one half of the whole or part of the body and limbs In this case there may also be asymmetry the limbs of the affected side being smaller than those on the sound side (hemiatrophy) The vessels in nævus flammeus may be barely visible or obvious capillaries or large purple venules perhaps with nodular excrescences

Course and Prognosis —Nævus flammeus usually persists for life, except for the transient form on the face Some of the darker port wine stains may become more irregular and scaly as time progresses

Treatment —If there is a diffuse pinkness without blood vessels visible to the naked eye a trial of thorium X applications is justified 1500 e s u in spirit being painted on at fortnightly intervals for about 12 applications Photographic control is advisable and if after 12 treatments there is little or no improvement, it is not justifiable to continue with this procedure Elevated areas may be destroyed and flattened with the galvano cautery For the rest cosmetic coverage offers the best prospects particularly in women Some cosmetic firms provide a service in large cities whereby patients with blemishes can by individual trial be supplied with a cover preparation most suited to their complexions In men the problem is more difficult and the patient may prefer to leave his lesion uncovered Plastic surgery is rarely feasible

NÆVUS VASCULOSUS (STRAWBERRY MARK CAVERNO CAPILLARY NÆVUS)

This has a characteristic natural history It may be present at birth or it may appear within the first 2 weeks of extra uterine life as a *bright red, flat or slightly raised* pinhead sized nodule which steadily enlarges until about 8 or 9 months of age, when its growth stops and its gradual regression begins, the lesion finally dis appearing without trace or with slight scarring at about 5 years of age

Sometimes these hæmangiomata develop on a markedly raised area of venous tissue but the ultimate prognosis is equally good Histologically there is vascular proliferation in a fibrous or fatty stroma

Strawberry nævi may occur anywhere on the skin but rarely cause serious incon venience unless they involve the mouth or the anus an ear or a finger Large hæman giomata or those at sites exposed to trauma or a great deal of movement may become ulcerated and infected

Treatment —Simple capillary and caverno capillary hæmangiomata are best left to run their natural course which ends in resolution at about 5 years of age Periodic inspection and measurement or photography with reassurance of the mother are usually sufficient It is wise to inform the mother that a waiting policy will give the best results in the long run whereas any interference will cause some scarring and, if the lesion is on the scalp loss of hair Radiotherapy of a strawberry nævus near the nipple of a female infant is likely to be followed by nondevelopment of that breast and irradiation of a lesion near a joint may interfere with the growth of a limb Applications of carbon dioxide snow made in the first few months while the hæmangi oma is growing may be followed by a ring shaped recurrence around the scar

If there is ulceration infection should be controlled with a *suitable antibiotic* and the lesion subsequently dressed with tulle gras until the ulcer is scarred over If hæmorrhage occurs it can be controlled by a pressure pad

Rapidly growing hæmangiomata around the mouth may have to be treated, injections of hot water or sclerosing chemicals excision or radiotherapy can be used, *depending on what is considered most suitable*

STELLATE HÆMANGIOMATA

These small spider nævi appear on the face or hands in young children They may become much more numerous in pregnancy and in the presence of liver disorders There is a central venule with radiating capillaries

Treatment —The galvano cautery point is applied cold to the central vessel the current is switched on and the point withdrawn when the patient flinches

SENILE HÆMANGIOMATA (CAMPBELL DE MORGAN SPOTS)

These pinhead sized or larger red spots occur more and more after the age of 40 particularly on the trunk and face On the scrotum they often have a rough surface (angiokeratomata) They have no significance as regards the general health and need no treatment

FAMILIAL HÆMORRHAGIC TELANGIECTASIA (OSLER)

In this disorder numerous hæmangiomata and telangiectases occur on the skin and mucous membranes the latter may cause hæmorrhages from the nose mouth stomach kidneys vagina or rectum

Treatment —Individual lesions can be destroyed with the galvano cautery

ANGIOKERATOMA (MIBELLI)

These are warty angiomata which occur on the extremities of young subjects

Angiokeratoma corporis diffusum are similar lesions but with rather less wartiness on the trunk and external genitalia There may also be proliferation of Bowman s capsules in the renal glomeruli of the vascular musculature and of the heart muscle

GRANULOMA TELANGIECTATICUM (GRANULOMA PYOGENICUM)

This is a rapidly growing hæmangioma which soon becomes eroded and infected It presents as a pink shiny orange pip sized exuding and bleeding nodule Histo logically there is great proliferation of capillaries and of fibroblasts

Treatment is by galvano cautery destruction

GLOMUS TUMOUR (GLOMANGIOMA)

These very painful nodules are formed from the neurovascular glomus an arterio venous anastomosis They are usually single flat or raised lesions on the finger tip nail bed or occasionally elsewhere for example on the forearm

Treatment is by wide excision

LYMPHANGIOMA

Lymphangiomata may be circumscribed and superficial or widespread cavernous and deep In the former translucent superficial lemon coloured or red vesicles are present in a group at birth or soon after The surface of the vesicles may be slightly warty Histologically there are dilated lymph spaces

Treatment is unnecessary but excision is sometimes performed

In lymphangioma cavernosum there is also hypertrophy of the connective tissue *causing macrocheilia macroglossia or enlargement of part or the whole of a limb* In this form treatment other than drastic surgery is rarely possible

JUXTA ARTICULAR NODES

These are painless firm subcutaneous fibrous nodules occasionally found near the elbows or knees or other joints in tertiary syphilis Non syphilitic juxta articular nodes also occur as in acrodermatitis chronica atrophicans (Pick Herxheimer)

PARAFFINOMA

Paraffinoma is a nodular fibrotic subcutaneous thickening somewhat resembling morphœa but due to injection of paraffin or camphorated oil the former sometimes

having been used in an attempt to iron out creases and saggings in the ageing skin and the latter having been used as a vehicle for certain subcutaneous injections

Histologically there is a "Swiss cheese" appearance of cavitation indicating where the oily substance was contained and around these spaces is an inflammatory and foreign body giant cell reaction with fibrosis The presence of the oil within the spaces can be demonstrated in frozen sections

Diagnosis is from lipophagic granuloma and morphœa on histological grounds

Treatment is difficult and usually inadvisable Sometimes excision and grafting is justifiable

CUTANEOUS RETICULOSES

MALIGN RETICULOSES

These serious systemic infiltrative disorders may be ushered in by general pruritus furunculosis, nonspecific eruptions urticarial pruriginous and eczematised lesions parapsoriasis en plaque, poikiloderma purpura erythroderma or cutaneous or subcutaneous obtuse dome shaped plum coloured or skin coloured nodules which may ulcerate When large tomato tumours form the clinical description of "mycosis fungoides" is sometimes used It is at present not possible satisfactorily to classify these maladies

Pathology—Biopsy from the cutaneous nodule shows a polymorphic infiltrate in Hodgkin's disease and mycosis fungoides The Sternberg Reed giant cells are pathognomonic of Hodgkin s disease and in the infiltrate there are also neutrophils many eosinophils plasma cells, histiocytes fibroblasts and immature reticulum and stem cells

In mycosis fungoides the infiltrate is similarly polymorphic but Sternberg Reed cells are absent Small accumulations of lymphocytes and histiocytes are present in the epidermis (Pautrier micro abscesses)

Clinical Forms—Hodgkin s disease may present with pruritus *furunculosis* a nonspecific eruption or tumours or ulcers having the specific pathology of the disease Tumours on the face may give a leonine appearance

In lymphatic leukæmia erythroderma (l homme rouge) is the commonest form but this may be preceded by pruritus and nonspecific eczematoid *lesions by* parapsoriasis en plaque and poikiloderma or by itchy pink plaques resembling urticaria The leukæmia may develop late in the course of the disease Large *fungoid* tumours may form (mycosis fungoides) with or without leukæmia Infiltrative skin lesions have also been described in monocytic leukæmia and rarely in myeloid leukæmia

Course and Prognosis—These maladies are all fatal after *intervals* varying between a few months and several years Death is usually due to pulmonary complications marrow destruction or involvement of other organs

Diagnosis—Reticulosis must be considered a possibility *in all persistent* forms of generalised pruritus furunculosis nonspecific eruptions parapsoriasis en plaque poikiloderma erythroderma tumours and ulcers of the skin Often the diagnosis can only be established after a long period of observation and *after repeated* biopsies

Treatment—General pruritus of Hodgkin s disease may be relieved by X irradiation of the epigastric region Erythroderma may be subjectively relieved by corticotrophin Earlier more superficial plaque *like erythematous* infiltration may respond well to weekly paintings with thorium X 1500 e s u per ml for as many treatments as may be necessary The tumours are usually radio sensitive at first responding to two or *three exposures* of 250 r each at weekly intervals As the disease progresses the tumours tend to become more and more radio resistant

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BENIGN RETICULOSES

FOLLICULAR LYMPHOCYTOMA (LYMPHADENOSIS BENIGNA CUTIS, SPIEGLER FENDT SARCOID)

This occurs as one or more dome shaped nodules on the scalp face, ears nose, breasts genitalia or elsewhere

Pathology—The nodules consist of nests of lymphocytes

Course and Prognosis—There is some doubt about the benignity of this condition It is believed that after years the condition may develop into a fatal reticulosis

Treatment—The lesions usually flatten and disappear after two or three X ray exposures of 250 r each at weekly intervals

MILIARY LYMPHOCYTOMA

This is a condition of pinhead sized translucent nodules in groups which arise on the malar region or forehead Each consists of a circumscribed nest of lympho cytes The condition is not a reticulosis but is apparently an unusual reaction to light

Treatment is ineffective Light screening creams should be prescribed if only to prevent worsening

DISEASES OF THE HAIR

CONGENITAL CONDITIONS OF THE HAIR

These include pili torti (spiral twisting of the hair) monilethrix (beaded hair, the shaft being constricted with absence of the medulla at regular intervals as a result of which the hair breaks off short) congenital ectodermal defects in which the scalp hair may be delicate and fine or woolly or absent (congenital alopecia) In albinism the hair is white

ACQUIRED CONDITIONS OF THE HAIR

CANITIES (WHITENESS OF THE HAIR)

This may be physiological from the age of about 40 years onwards It may also be pathological and premature in endocrine disorders including hyperthyroidism and Simmonds disease There may be partial or general whitening of the hair that regrows after alopecia areata or in the involvement of hairy areas by vitiligo The hair may also become white after severe emotional disturbance

Treatment is by suitable dyes which may be of the harmless type for example henna or potentially harmful for example paraphenylenediamine Before using the latter a patch test should be performed to determine the presence or absence of sensitivity to the chemical It should never be applied to a scalp on which any cuts, abrasions scabs or redness exist

NON CICATRICIAL ALOPECIA (BALDNESS)

This may be local or general all the hair may be lost from a given area or there may be sparseness of the hair on the site (alopecia diffusa)

Alopecia areata is a complete loss of hair from a circumscribed area of the scalp or the beard More extensive forms result in the loss of all the hair from the scalp (alopecia totalis) and in the worst cases the hair of the beard lashes and brows axillæ and pubis and even the glabrous hair may fall (alopecia universalis)

Ætiology and Pathology—The cause is unknown but emotional factors are

prominent in about two thirds of the cases The condition may represent an hysterical symbolisation Histologically there is an inflammatory infiltrate around the hair follicles which leads to atrophic changes of variable degree after the milder forms, regrowth of hair may occur but after the severer forms the loss may be permanent. In long standing alopecia, the inflammatory infiltrate is absent and the follicular atrophy more marked

Clinical Pictures —In simple alopecia areata, there are oval or circular completely bald shiny patches which by confluence may form polycyclic areas There is no sign of inflammation and an absence of scurf At the margin of recent and extending patches " exclamation mark (club shaped) hairs are visible These are short hairs with their ends of greater diameter than the portion level with the surface of the skin First attacks of the condition often occur in children and young adults Ophiasis is a variety of alopecia with serpentine lesions

Course and Prognosis —Recovery is usual from first attacks and localised lesions but becomes increasingly unlikely with each recurrence Sometimes one patch develops while another is regrowing The band like forms affecting the occipito temporal regions and alopecia totalis are of poor prognosis When regrowth occurs the new hair is at first fine and often white

Diagnosis —In children alopecia areata has to be differentiated from tinea capitis and from trichotillomania Tinea capitis presents as scaly patches with short broken hairs looking thicker than the adjoining healthy hairs and with frayed ends The inflammatory reaction may be insignificant or frankly folliculopustular Wood s light examination and microscopy makes the diagnosis clear The black dot ' ringworm due to *T violaceum* in which the hairs break off flush with the surface of the skin may resemble a regrowing alopecia Microscopy is necessary for the differentiation Trichotillomania an habitual tugging twisting and manipulation of the hair, is usually situated in the frontal or temporal regions the hair loss is only partial and a history of hair tugging will be obtained if the parent is asked this question

In adults alopecia areata has to be differentiated from various forms of cicatricial alopecia (*q v*)

Treatment is supportive A stimulating liniment may be rubbed in daily or a second degree erythema exposure to ultra violet irradiation given once a week Psychotherapy is seldom effective Foci of sepsis and eyestrain are no longer regarded as of ætiological significance

The term *alopecia diffusa* implies a diffuse thinning of the hair over part or the whole of the scalp

Androgenic alopecia is the commonest variety, occurring in most males from about the age of 40 onwards and in some as early as 20 years of age The hair becomes thinner and finer in the bifrontal and vertical regions but remains in its former texture and thickness on the rest of the scalp Genetic (racial and familial) influences are important in its ætiology also the fineness of the hair There is at present no means of checking its progress except by control of the coincident scurf or mildly infective folliculitis (*q v*) Massage may do more harm than good and ultra violet irradiation has no effect Œstrogens too in practical doses are ineffective

Women also are sometimes affected with this type of hair loss after the menopause and there may also be hirsutes of male distribution Occasionally alopecia of androgenic type occurs after pregnancy in these circumstances non destruction of androgens by the liver is suspected as the cause

In *myxœdema* the hair over the whole scalp is thinned fine dry limp and lustreless but may recover some of its former texture by suitable dosage with thyroid extract

In *nutritional deficiencies* particularly of vitamins A and C the phrynodermatous process may involve the scalp causing loss of hair and a finer texture of those that remain

Defluvium capillorum is a term used for conditions of temporary or permanent occasional or recurrent falling of the hair from causes known or unknown including acute infections, emotional stresses, exfoliative dermatitis toxic processes and nutritional deficiency states acting indirectly through endocrine and metabolic mechanisms

In *infective* (*seborrhœic*) *dermatitis* the hair loss of masculine distribution that is so often present is accentuated by the folliculitis

In *secondary syphilis* there may be an irregular but diffuse loss of hair, giving a moth-eaten " appearance to the scalp

X irradiation is often used to bring about epilation of patients suffering from ringworm of the scalp A single X ray exposure of 400 to 450 r causes shedding of the hair after 3 weeks with complete regrowth starting in another 3 weeks Further exposures or a single exposure of more than 450 r may cause permanent epilation, with the development after a few years of the picture of chronic radiodermatitis (atrophy telangiectasia pigmentation and depigmentation)

Certain toxic substances have a direct action on the hair papillæ One of these, thallous acetate was used some years ago to bring about temporary epilation but its use has been almost completely abandoned owing to the small margin between the therapeutic and the toxic dosage the latter causing albuminuria blindness, coma and even death The use of this substance is strongly to be deprecated

FRAGILITAS CRINIUM

Breaking of the hairs at various distances from the scalp must be differentiated from defluvium capillorum The hairs show frayed and split ends and sometimes frayed nodose swellings on their shafts (trichorrhexis nodosa) The cause is undue drying and degreasing of the hair which may follow the excessive use of shampoos Bleaching agents may also be responsible The treatment is preventive by avoidance of these substances in excess Once it has occurred it may be helpful to prescribe a lotion of salicylic acid 2 per cent. oil of rosemary 2 per cent castor oil 12½ per cent in industrial spirit, for use as a hair dressing

PILI INCARNATI

Ingrowing hairs resembling folliculitis barbæ of mild degree (*q v*)

CICATRICIAL ALOPECIA

Scarring baldness has a large number of causes including

- Physical traumata—cuts burns X rays radium
- Chemical traumata—caustics etc
- Exanthemata—variola varicella zoster
- Drug intoxications—lichenoid mepacrine eruption
- Fungous infections—kerion favus
- Granulomata—syphilis lupus sarcoidosis leprosy halogen eruptions
- Reticuloses—lymphocytomata or lymphoblastomata Hodgkin s disease
- New growths—rodent ulcers
- Nævoid conditions—nævus sebaceus hydrocystadenoma papilliferum (both present as bald areas with yellowish papillomatous outgrowths)
- Skin diseases—lupus erythematosus lichen plano pilaris morphœa folliculitis decalvans acne varioliformis pseudo pelade

A few of these may be described in some detail

Radiogenic alopecia presents as poikiloderma that is a polymorphic and patchy picture of atrophy telangiectasia depigmentation and hyperpigmentation It is occasionally seen in patients who have been treated by X rays for ringworm of the

scalp in childhood The condition is irreversible and after several years keratoses and squamous carcinoma may develop

Varicella variola and zoster may show macular bald areas at the sites previously occupied by the vesicles

The lichenoid gold or mepacrine dermatosis presents as one of its features a patchy folliculitis of the scalp, beard eyebrows and lashes which is followed by baldness either temporary or permanent The history of drug treatment and the lichenoid features elsewhere help to supply the correct diagnosis

Favus may present with scutuliform crusts with an offensive odour or as folliculitis decalvans (*q v*) Affected hairs fluoresce pale blue under Wood s light and spores and mycelium are visible within the hair shafts on microscopic examination

Syphilis in addition to the ' moth eaten alopecia at the secondary stage already mentioned, may in the tertiary stage cause cicatricial alopecia at the sites of gummata which in this situation often develop a heavy secondary infection

Leprosy may give rise to baldness in its nodular and in its maculo anæsthetic forms

Lupus vulgaris rarely involves the scalp and when it does the face is usually heavily affected as well with the characteristic 'apple jelly' nodulation

Reticuloses may cause obtuse skin or plum coloured dome shaped swellings with baldness on the scalp or occasionally more diffuse pink infiltrated nodulation

Rodent ulcer when it affects the vertex, differs considerably from the button like lesions seen on the face The scalp lesions are flat or even slightly depressed scleroderma like plaques perhaps with some crusting around the edges which also have a slight translucency and pearly appearance

Lupus erythemato us causes red bald patches with central atrophic carring and marginal infiltrated redness with follicular plugging and adherent scales

Lichen plano pilaris causes irregular areas of baldness and itchy acuminate violaceous follicular papules with shiny tops

Morphœa causes an oval or linear waxy shiny, bald area with a lilac halo

Folliculitis decalvans is a coccal folliculitis causing atrophy of the follicles and atrophic scarring with baldness Often the central area is bald apart from a few scattered hairs but shows no active inflammation towards the margin of the bald area are scaly follicular papules and sometimes a few pustules The condition can be controlled to some extent by appropriate antibiotics

Acne varioliformis leaves depressed hairless scars around the hair margin

Pseudo pelade presents a irregular and angular areas of scarred baldness with tufts of hair remaining amidst the bald patches The condition sometimes represents the end stage of lichen plano pilaris of the scalp

Ulerythema ophryogenes is a rare scarring folliculitis of the eyebrows of uncertain ætiology Sometimes it may be a manifestation of lupus erythematosus sometimes of coccal folliculitis profunda (sycosis)

Perifolliculitis capitis abscedens et suffodiens is a rare condition of fluctuant swellings on the scalp with sinuous tracks multiple sinuses and considerable loss of hair Culture may be sterile The condition is analogous to hydradenitis suppurativa and is most difficult to relieve It may be necessary to open up the tracks and allow them to heal by granulation

HYPERTRICHOSIS (HIRSUTES)

The localised form occurs as coarse hairs growing from a mole which is usually small and nodular but sometimes extensive and plaque like They rarely need treatment unless they occur on exposed surfaces when the patient may ask for something to be done on cosmetic grounds One of two courses should be adopted—either the hairs are destroyed individually by electrolysis or the whole mole is excised and

wound stitched or grafted Interfering traumatic procedures such as cautery or carbon dioxide snow freezing are to be deprecated the cosmetic results are poor and the depth of the lesions means that only excision can remove it all

Very rarely local hirsutes occurs over the sacrum without pigmentation, apparently as a vestigial tail

General hypertrichosis involves the areas of masculine coarse hairs the upper lip and beard area, the chest mid line of abdomen and subumbilical triangle and the extensor surfaces of the limbs Gross hypertrichosis is sometimes a source of embarrassment in the male in the female minor degrees may be equally distressing

Ætiology —The majority are genetic (racial and familial) in origin and no doubt related to a functional endocrine imbalance which is at present, incapable of adjustment. If the moon face obesity purple striæ hypertension and glycosuria are present (Cushing s syndrome) investigation should be made for pituitary or adrenal cortical neoplasia

The administration of adreno corticotrophic hormones may bring about acne and hirsutes

Acne vulgaris is often accompanied by hirsutes of moderate degree

Treatment —If there is no hypertension glycosuria moon face striæ or obesity and normal 17 ketosteroid excretion the condition can be regarded as genetic and is a functional endocrine disorder incapable (at present) of relief except by local epilatory methods

For coarse hairs electrolysis carried out by an expert gives the best results but in inexperienced hands noticeable pinpoint scarring may follow If the hirsutes is widespread and finer electrolysis entails many tedious treatments and it is better to use some simpler method of masking the condition Bleaching with peroxide of hydrogen (neutralised) followed by exposure to daylight is often valuable Shaving is often the ideal method and does not as is supposed by some lead to coarsening of the hair Unfortunately it carries with it a discouraging sense of performing a masculine act and many women refuse this suggestion for that reason although they are prepared illogically to use pumice the equivalent of pre historic man s razor Chemical depilatories are more useful in the axillæ than on the face where any inflammatory reaction they might cause would be more unfortunate

Epilation by wax has a small sphere of utility for localised patches as a temporary measure Plucking too is commonly performed for this purpose but, if persisted in may end in some traumatic epidermal proliferation of the ostia of the follicles

X rays should never be used for cosmetic epilation of women s faces breasts or limbs because of the likelihood of chronic radiodermatitis developing and of subsequent keratoses and epitheliomata

DISEASES OF THE NAILS

The nails may be affected in various ways by local or general conditions congenital or acquired

PARONYCHIA

Paronychia or inflammation of the nail fold is due to micro organisms gaining entry through a break in the cuticular barrier and it may be acute or chronic

The *acute* form (paronychial whitlow) due to coccal infection presents as a red tender, cushion like swelling on one or both sides of the nail fold Yellowish discoloration due to pus formation is soon apparent A painless epidermal variety may be the unsuspected source of various staphylococcal infections of the skin

Treatment is by systemic penicillin in the earliest stage or by avulsion of the nail and a paronychial flap at the later stage The epidermal variety is easily dealt with by removal of the overlying epidermis and cleansing with 1 per cent cetrimide

If a paronychial whitlow persists neither resolving nor suppurating, consideration should be given to the possibility of its being an example of *Hutchinson's melanotic whitlow* (onychia maligna), a highly malignant condition masquerading as an infection and necessitating amputation (see Melanoma)

Chronic paronychia like the acute form is due to destruction of the protective cuticle on the nail plate This happens following the use of powerful detergents strong alkalis and soaps constant exposure to water, the use of cuticle removers and clumsy manicure Through the gap thus made pass detergents soaps alkalis and water which cause a chemical paronychia with alkalinity of the fold this predisposes to infection by organisms normally present on the skin such as monilia and *Staphylococcus saprophyticus*

The condition presents as persistent reddened cushion like swellings around the nail fold with a space between the fold and the nail into which a probe can be passed for a few millimetres There may be occasional exacerbations with a slight discharge of thin pus The nail plate is usually deformed (onychia) by irregular transverse ridging and grooving, with some discolouration Sometimes a nail becomes detached from its bed

Course and Prognosis —Untreated, the condition tends to persist indefinitely

Treatment —Wet work and the use of detergents and alkalis must be reduced to a minimum Rubber gloves if used should be worn for not more than 10 minutes at a time A water repellent barrier cream may be applied around the folds immediately before doing any essential wet work

Active treatment consists of the application of pigmentum magentæ to the nail fold twice a day by means of a camel hair brush This may succeed in the milder cases but in more severe ones a course of X irradiation (150 r fortnightly up to a total of 600 r) is often most effective

The patient must continue to take precautions against damage to the cuticle after the condition has healed

Tuberculous paronychia is very rare Its treatment is the same as that of cutaneous tuberculosis elsewhere

INGROWING TOE NAIL (UNGUIS INCARNATUS)

This nearly always affects the great toe and is due to a faulty technique of cutting the nail whereby a lateral sharp spur is left which cuts into the flesh tight socks and shoes also play a part The condition presents as a painful swollen area to one side of the toe near the free edge of the nail A purulent infection is common or a granulomatous condition

Treatment —In the early stages corrective chiropody may be sufficient but once a purulent or granulomatous condition has developed it is necessary to remove half the nail and to excise a wedge of tissue at the site of ingrowth to enable the nail to grow without cutting into the flesh

Hangnails are skin tags alongside the nail the result of faulty manicuring a tic or chapping The tag as it tears becomes of increasing depth The diagnosis is from paronychial warts (*q v*) The treatment is to cut off the tag and to apply an antiseptic and a collodion dressing

Subungual hyperkeratosis is usually due to psoriasis dermatitis or some other skin disorder Tinea must be excluded by microscopic examination

Subungual exostosis presents as a painful swelling beneath the nail, with some

hyperkeratosis The condition is differentiated from a subungual wart by X ray examination and the treatment is surgical

Subungual warts (see Warts)

DISORDERS OF THE NAIL PLATE

Affections of the nail plate, secondary to disease of the matrix are many and various The nails may undergo atrophy or complete destruction (acquired anonychia) or hypertrophy, the latter either as a simple thickening following trauma (onychauxis) or as ram s horn like masses (onychogryphosis or ' claw nails) For convenience the thickened nails may have to be removed but the new nails will be just as thick Excision of the nail beds is sometimes advisable but it is a delicate surgical procedure to remove all the bed proximally and laterally without opening the distal interphalangeal joints

Congenital abnormalities include absence of the nails (anonychia) rudimentary nails ectopic nails (onychoheterotopia) spoon shaped nails (koilonychia) extreme thickening (pachyonychia congenita)

Tics affecting the nail and its surrounds include nail biting (onychophagia) and picking (onychotillomania) one form of hangnail and knuckle chewing

Dystrophy (dullness and roughening) of the nails may be due to ringworm psoriasis dermatitis lichen planus syphilis tuberculosis leprosy or unknown causes Ringworm should always be suspected when one or a few nails are discoloured, irregular friable or honeycombed Microscopy repeatedly if necessary enables the diagnosis to be confirmed

Psoriasis of the nails usually occurs with psoriasis elsewhere so that the diagnosis is simple but it may affect the nails alone It presents as thimble pitting of the nails there being anything from a single pit to uniform involvement of all the nails In its more severe forms it causes yellow opaque brittle thickening of the nails usually distally or laterally sometimes over the whole plate The nails may be raised and shed by psoriasis of the nail bed

Dermatitis around and in the nail folds leads to pitting and transverse or longitudinal grooving of the nails

When dystrophy of the nails is not explicable as of fungous psoriatic or dermatitic origin the Wassermann reaction should be tested and examination directed especially to evidence of syphilis or of lichen planus elsewhere Median canaliform dystrophy is a permanent thickened ridge running along the centre of the nail and due to previous chemical or physical trauma to the part of the matrix supplying this portion of nail

Splitting of the nail tips into lamellæ (onychoschizia) is usually caused by powerful detergents or alkalis, occasionally nail manicure preparations and varnish removers are responsible

Transverse groovings and ridgings of the nails are spoken of as Beau s lines They may arise *in one or more nails from dermatitis psoriasis and other skin conditions* or they may indicate some recent illness for example pneumonia which has led to a temporary impairment of the nutrition of the nail They take about 6 months to grow out and from their situation on the nail the date of previous ill health can be roughly estimated

Longitudinal grooving and ridging of the nails is very common and of no significance in minor degrees but when severe and accompanied by *splitting of the nails* it is dignified by the name of onychorrhexis and attention should be paid to the avoidance of degreasing and dehydrating substances

White spots on the nails (canities unguium or leuconychia) are of no diagnostic significance or import except that they indicate areas of imperfect cornification possibly the result of injury

Longitudinal bands of variation in colour either lighter or darker may result from local pigmentary changes in the matrix

Koilonychia may be congenital and of no serious import When acquired it often indicates a chronic malnutrition of the matrices *from iron and vitamin B deficiency* A general cause cannot always be found and local ischæmic proces es are ometimes *responsible* Damage to one or more fingers may cause a somewhat similar deformity except that the nails are not thin as they *are in nutritional* koilonychia

Clubbing of the fingers includes an increased curvature of the nails both in the longitudinal and transverse axes and an increased springiness of the nails on their beds *It is* associated with suppurative lung conditions and cyanotic congenital heart disease etc There is often also hypertrophy of the distal phalanx (hypertrophic pulmonary osteoarthropathy)

Detachment of the nail from its bed may start proximally (onychoptosis) from hæmatoma or paronychia or distally (onycholysis) as in psoriasis Onychomadesis is a term applied to shedding of all the nails (sometimes recurrently) starting proximally The causes of this phenomenon include vasospastic states skin diseases beneath the nails for example exfoliative dermatitis or psoriasis chemical contact injury syphilis diabetes or scarlet fever in its peeling stage

Usure des ongles is a term applied to wearing away of the free border of one or more nails as the result of occupational friction or even merely rubbing with the finger tips

CONDITIONS OF THE NAIL BED

Conditions of the nail bed observed through the plate include the splinter *hæmorrhages*' of lupus erythematosus, purpura hæmatomata cyanosis stains of various chemicals and racial pigmentation

DISEASES OF THE LIPS AND MOUTH

The lips and mouth are affected in many skin diseases which have been described elsewhere It remains to describe a few other conditions affecting the lips and mouth

CHEILITIS

Commissural cheilitis (angular stomatitis) causes redness, slight crusting and fissuring It may be a form of infective (flexural) dermatitis or a manifestation of deficiency of iron and vitamin B or due to falling in of the angles of the mouth and a resultant extension of the moist surface, arising from lack of teeth or from dentures which are too narrow and shallow or it may be due to salivation resulting from hypersensitivity to vulcanite or acrylic denture material to tooth paste mouth wash or fruit juices It should be remembered that frambœsiform syphilides may develop in this situation or at the cleft of the chin

Cheilitis exfoliativa is a peeling of the vermilion surface of the lips u ually due to contact with a sensitiser In severe forms there is œdema, vesiculation and cru ting, perhaps going on to fissuring Eosin in lipstick is the commonest cause this may act either by causing a contact eczematous reaction or by causing sensitisation to ultra violet rays In the former both lips may be affected In the latter the lower lip alone suffers Rarer causes include nail varnish tooth paste mouth washes fruit juices essential oils nicotine mentholated cigarettes chemicals handled at work and a lip sucking and chewing habit

Cheilitis glandularis is a rare condition of unknown cause The mucous glands are enlarged and there is a glairy exudate with some crusting Treatment is by cautery destruction of the swellings

Macrocheilia may be congenital or acquired The latter is usually due to lymphatic obstruction secondary to streptococcal cellulitis the infection gaining entry through

a fissure but syphilis and tuberculosis are also sometimes responsible for this elephantiatic condition

Conditions of the lips dealt with elsewhere include lupus erythematosus lichen planus psoriasis keratoses leucoplakia urticaria erythema multiforme, granuloma pyogenicum syphilis tuberculosis recurrent herpes and tumours Mucous (retention) cysts occur on the mucosal aspect

STOMATITIS

Inflammation of the mouth may cause diffuse redness erosions blisters submucosal hæmorrhages or ulcers *The tongue may exfoliate In more chronic forms redness* is inconspicuous and there is leucoplakia

Ætiology —Lesions appear in the mouth in infections with syphilis tuberculosis streptococci monilia Vincent s angina herpes simplex zoster varicella variola etc. Lesions also appear in intoxications by many drugs (*q v*) and heavy metals Nutritional deficiencies (scurvy pellagra) cause hæmorrhage and inflammation Blood disorders such as leukæmia agranulocytosis pernicious anæmia hæmophilia metabolic disorders such as diabetes mellitus and uræmia may all cause lesions in the mouth Finally certain idiopathic skin diseases may be responsible particularly lichen planus lupus erythematosus erythema multiforme pemphigus Behcet s syndrome Lipschütz disease and rare maladies such as epidermolysis bullosa Darier s disease and acanthosis nigricans

Syphilis —Primary lesions may occur on the lip tongue palate or tonsil and mucous patches and snail track ulcers may appear anywhere in the mouth Gummata may develop in the palate or tongue or there may be a syphilitic glossitis with irregular leucoplakia

Tuberculosis (see page 1241)

Streptococcal stomatitis may complicate tonsillitis There is a patchy or generalised cherry red and swollen condition of the gums

Monilial stomatitis (thrush) produces soft white rapidly spreading raised patches This malady may develop in infants or in adults who are taking antibiotics or using antibiotic mouth washes

Vincent s angina due to symbiosis between a spirochæte and fusiform bacillus causes grey patches in a red raw bleeding surface it particularly affects the gingivo-buccal margin or gingival sulci Gangrenous stomatitis (cancrum oris) is a very rare form of Vincent s infection in extremely debilitated children

Herpetic stomatitis first affects infants 2 to 3 years old This primary infection may be followed by a delicately balanced host virus relationship with recurrences of aphthous stomatitis when debilitated There are painful swollen erosions (aphthæ) on the cheeks gums or tongue

Zoster (see p 1247)

Varicella (see p 1248)

Variola (see p 160)

Stomatitis medicamentosa —Iodides may cause hæmorrhages or bullæ many other drugs may cause bullæ erosions ulcers and lesions resembling lichen planus or erythema multiforme (see Drug Eruptions)

Stomatitis due to heavy metals —Mercury in sufficient dosage causes salivation with gross swelling of the gums and tongue often accompanied by nephritis Lead causes a blue black discolouration of the gums opposite areas of marginal gingivitis (pyorrhœa) There may also be ulceration Silver causes a blue grey pigmentation or an increase of melanin pigmentation Bismuth may cause a similar discolouration and gold may cause stomatitis and pigmentation These metallic pigmentations have to be differentiated from that of Addison s disease and racial pigmentation which may occasionally be seen on the gums of white persons with some coloured ancestry as well as in the mouths of coloured people

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GLOSSITIS

Ætiological factors in this condition are alcohol smoking condiments and gastro intestinal and metabolic disorders (Plummer Vinson syndrome sprue pellagra, pernicious anæmia diabetes mellitus) Electrogalvanism from metals of different electro-potentials in dental prostheses can cause a metallic or salty taste salivation tingling shocks eroded gums or tarnished teeth

Moeller s glossitis (glossodynia exfoliata) is rare It chiefly affects women causing severe burning pain which makes feeding difficult There are red patches of denuded filiform papillæ and white leucoplakic nodules

Glossitis rhomboidea mediana is a lozenge shaped elevation in the mid line about the middle third of the tongue well defined anteriorly but fading posteriorly into the circumvallate papillæ It is due to the persistence of the tuberculum impar and is of no serious significance but is sometimes discovered accidentally by the patient who may think it is cancerous

Glossodynia —This may be symptomatic of irritation from heat alcohol or trauma of avitaminosis pernicious anæmia leukæmia drug intolerance (especially phenol phthalein) electrogalvanism xerostoma or cancerphobia It may also occur from changes in the temporo mandibular joints, usually due to lack of teeth resulting in abnormal stresses on these joints

Lingua geographica is often accompanied by soreness In this idiopathic condition there is a wandering superficial exfoliation which slowly changes its distribution day by day producing reddened denuded areas It is benign and patients fears of cancer can be allayed with confidence Treatment is palliative with normal saline mouth washes or, better still by ignoring it It tends to persist indefinitely

Lingua plicata (scrotal tongue) is a congenital malformation of deep sulci running in various directions Its significance is that it may lead to accumulations of food debris in these folds Careful hygiene is advisable perhaps using a wool tipped probe to clean out the sulci

Lingua nigra has two forms The black hairy tongue is an hypertrophic condition of the filiform papillæ giving the centre of the tongue in its anterior third an appearance like a black dog s matted coat The use of antibiotics may aggravate it by encouraging the growth of yeasts in the interpapillary spaces The non hairy black tongue may be caused by chewing tobacco or tooth paste dyed sweets certain drugs chromogenic bacteria fungi or metallic sulphides The tongue is dark in Addison s disease

Tumours of the tongue include papilloma carcinoma hæmangioma and lymphangioma lipoma fibroma sarcoma chondroma and mucous cysts

Macroglossia occurs in primary systemic amyloidosis and lingual keratoses in some cases of Darier s disease

BRIAN F RUSSELL

TROPICAL SKIN DISEASES

Introduction —*In the tropics and subtropics skin diseases* are of major importance In addition to those which are peculiar to hot countries the skin diseases of temperate climates are commonly encountered there and for a variety of reasons often assume more serious significance This was very evident in white troops fighting in the tropics in the War of 1939–1945

Skin texture and pigmentation are important, and generally fair skinned blond individuals do not stand hot climates as well as dark complexioned people Albinism and acquired leucoderma are both associated with lack of protective pigment in the skin and depigmented areas especially in fair complexioned individuals and may

Scurvy causes swelling redness and friability of the gums and purpura or hæmorrhage In *pellagra* the tongue is centrally stippled beefy and raw at the narrow tip and sides In *leukæmia* and *agranulocytosis* there may be purpura hæmorrhages and secondary infection, in *pernicious anæmia* the tongue is smooth and glazed, in *hæmophilia* hæmorrhages may occur within the mouth In untreated *diabetes mellitus* the tongue is large red dry glazed and fissured and there may be gingivitis In *uræmia* there may be oral ulceration and gingivitis *Lichen planus* has been described elsewhere buccal lesions occur most commonly and the lips gums and tongue may also be affected in this malady *Lupus erythematosus* occasionally affects the mucosal aspects of the cheeks, there are shiny red eroded areas with ulceration and leucoplakia

Erythema multiforme (see p 1257)

Pemphigus (see p 1288)

Behcet's syndrome begins with ulceration of the mouth ulceration of the genitalia or serious eye changes of conjunctivitis keratitis or hypopyon iritis One site may be affected months or years before the others There may also be nodules in the skin or acuminate papules The eye changes end in blindness The cause is unknown and there is no effective treatment Before the eyes are affected it is doubtful if this malady differs from periadenitis mucosa necrotica recurrens of Sutton or from ulcus vulvæ acutum recurrens of Lipschutz both of which are described as causing ulceration of the mouth and vulva

Epidermolysis bullosa of the skin may be accompanied by eroded oral lesions which go on to leucoplakia

LEUCOPLAKIA

Leucoplakia (mucosal dyskeratosis) is chronic stomatitis

Ætiology and Pathology —Leucoplakia may be caused by physical or chemical irritation or it may be the result of various diseases within the mouth including lichen planus lupus erythematosus syphilis or drug intoxications

Histologically there is hyperkeratosis and parakerato is and slight acanthosis

Clinical Picture —Leucoplakia may be smooth irregular or verrucose The smooth type is common on the buccal mucosa and is relatively benign but on the lower lip it may be the precursor of carcinoma The irregularly raised and depressed form is often syphilitic and precancerous It occurs especially on the tongue and within the angles of the mouth The verrucose form also is potentially carcinomatous The habit of cheek chewing may cause a pseudoleucoplakic roughness and whitening just within the commissure

Diagnosis from lichen planus is sometimes difficult and in fact may not be possible even on histological grounds Lichen planus usually presents as polygonal white spots feathery streaks or foliate traceries and atrophy with slight depression of the surface is more likely to be present than elevation as in leucoplakia At the vulva leucoplakia may be secondary to friction Friction may also cause a white peeling condition with fissuring of the perineum and perianal region this however is not leucoplakia but lichenification modified by the moist flexural situation Leucoplakia only occurs on mucous surfaces The distinction is important because it is unnecessary to excise the white skin of the perineum and perianal region in such a case on the grounds that it is a precancerous condition on the skin as well as on the vulva Excision if it is carried out should be limited to the mucosa of the vulva

Treatment —Leucoplakia is best treated by bland applications such as normal saline mouth washes and hydrous ointment to the vermilion surface of the lip Smoking hot drinks and condiments are best avoided No further action is necessary except periodic inspection for the earliest evidence of neoplastic proliferation If this is seen excision of the affected area should be carried out forthwith Radiotherapy is inadvisable

and yeast like fungi have been incriminated but they are only merely secondary invaders According to O Brien sebaceous deficiency causes physical changes and closure in the keratin ring surrounding the sweat duct occlusion follows and rupture of the sweat duct and the formation of miliarial vesicles ensue each sweat gland involved is said to remain obstructed for some time after the acute attack has subsided

Symptoms —The eruption consists of small glistening superficial vesicles with a well marked red areola and inflamed red papules which feel like grains of sand it may involve the trunk limbs forehead and almost any part of the body The *pricking burning sensation and great itching may be sufficient to prevent sleep, and* secondary bacterial infection may result from scratching

O Brien records that repeated attacks of prickly heat may lead to extensive chronic sweat gland obstruction and tropical anhydrotic asthenia

Treatment —PREVENTIVE —Previous suntan, loose clothing and working or sleeping in air conditioned rooms or in the open air reduce the liability to prickly heat Only light clothing should be worn and when possible it should be changed twice daily Soap should be used with moderation when washing

CURATIVE —After a tepid bath the application of corrosive sublimate solution (1/1000) containing Eau de Cologne is helpful Alternatively the following lotion is useful ℞ acid salicyl gr 30 hydrarg perchor gr 2 Sp vini rect 2 oz Aq dest ad 6 oz Subsequently a dusting powder such as zinc oxide boracic acid and starch in equal parts or boracic acid and menthol, affords some symptomatic relief In chronic cases O Brien advises desquamation of the stratum corneum by daily applications of 10 per cent salicylic acid in 90 per cent alcohol for 2 or 3 days followed by inunctions of lanoline twice daily, and later once weekly to restore the lipoid deficiency

CRAW CRAW

A West African native name (Kra kra) applied to any itchy papular or pustular eruption of the skin

Ætiology —O Neill found filarial embryos in this eruption resembling scabies but they were probably *Microfilaria streptocerca* which Macfie has since commonly found in the skin of West African negroes There is still doubt regarding its ætiology

Symptoms —The papules are hard and horny occur chiefly in the limbs and are very itchy scratching and secondary infection lead to a pustular dermatitis with enlargement of adjacent lymph glands

Diagnosis —The condition must not be confused with scabies or coolie itch no acari are obtained and no burrows seen Cutaneous onchocerciasis has also to be differentiated

Treatment —Pustules are opened ulcers scraped and crusts removed then dis infected with 1 in 1000 sublimate solution or carbolic lotion and subsequently dressed with boric acid ointment

DESERT SORE

Synonyms —Veldt Sore

Definition —A chronic septic sore somewhat resembling impetigo contagiosa occurring on exposed hairy parts of the body and affecting individuals living in hot dusty arid regions the causative organism is generally a hæmolytic streptococcus

Ætiology —The disease has a widespread geographical distribution in hot dry, sandy or desert country being known as veldt sore in South Africa barcoo rot in Northern Australia and desert sore in Egypt Mesopotamia and Iraq where many thousands of troops acquired the disease in the War of 1914–1918 It was equally prevalent in the campaigns in Egypt Palestine and the Western Desert (1940–1943),

show abnormal cutaneous response to sunlight with vesicular inflammation Bright tropical sunlight is especially injurious in conditions of solar sensitivity such as lupus erythematosus Leucoderma has often a peculiar and sinister significance in dark skinned people not only on account of the great disfigurement it produces but also because of its superficial resemblance to the depigmented patches of nerve leprosy

Owing to the heat and humidity a considerable strain is placed on the sweat glands The relatively alkaline reaction of sweat favours secondary pyogenic infection as does the friction of soiled, sweat sodden clothing In arid desert country the skin becomes clogged with dust and the bites of blood sucking insects are specially prone to be associated with secondary bacterial infection Skin diseases which are often regarded as a contraindication to tropical service include severe ichthyosis, lupus erythematosus prurigo æstivalis seborrhœic dermatitis severe acne vulgaris leucoderma and psoriasis (Fergusson) Severe and recurrent attacks of miliaria rubra may necessitate the sufferer abandoning the tropics So may extensive tropical *anhidrosis which is characterised by a goose fleshlike* appearance of the *skin with* local failure of sweating O Brien regards this condition as resulting from chronic occlusion of the sweat glands following successive attacks of miliaria rubra and records that if more than 50 per cent of the sweat glands be blocked in this fashion a state of tropical anhidrotic asthenia results

Certain drugs which are used mainly or exclusively for the treatment of tropical disease may give rise to rashes The use of photosensitising drugs should be avoided *and the possibility of aggravating acne remembered* when using *emetine* bismuth iodide in amœbic dysentery The employment of mepacrine to prevent malaria may occasionally lead to tropical lichinoid dermatitis, it indicates an idiosyncrasy to the drug the administration of which should cease

The tendency for urticaria eosinophilia and other allergic manifestations to develop in individuals with systemic helminthic infestations should be always remembered Parasitic invasion of the skin may be associated with skin eruptions such as ground itch caused by ankylostome larvæ and swimmer s itch' by bilharzia and other cercariæ Similarly creeping eruption may result from migrating larvæ such as *Ankylostoma braziliense* or the larvæ of bot flies of the genus Gastrophilus Warbles or furuncle like lesions discharging fly larvæ may be produced by flies of the genus Hypoderma or Gastrophilus laying their eggs under the dermis

A variety of fungoid infections is common *in the tropics Their course* is liable to be complicated by secondary pyococcal infection and parasitic achromia due to depigmentary action of the fungus Secondary leucoderma is not uncommonly seen in fungoid infections in dark skinned natives

Again native customs may modify such conditions as keloid which is very prevalent in parts of Africa where the negroes often purposely irritate *wounds to* produce tribal markings of a keloid nature

Certain skin diseases *specially prevalent in or peculiar* to the tropics and sub tropics which have not been considered in previous sections are described below

PRICKLY HEAT

Synonyms —Miliaria rubra Lichen tropicus

Definition —Prickly heat is an acute form of heat rash associated with excessive sweating in hot humid climates

Ætiology —It particularly affects Europeans of obese diathesis has a predilection for the covered parts of the skin *especially where there is friction from the clothes* and rapidly disappears on leaving the tropics by aeroplane or in cool weather Probably *it results from* a mechanical blockage of the ducts of the sweat glands with keratin or sodden inadequately cornified cells of the stratum corneum Bacteria

deep ulcers exist in the vicinity of joints The sores should be cleansed treated with a 1/1000 solution of aminacrine (5 amino acridine) and covered with non adhesive dressing such as " tulle gras ', which is coarse curtain net impregnated with petroleum jelly (99 per cent) and balsam of Peru (1 per cent) The application of Flavogel—a water soluble preparation of aminacrine in starch and tragacanth—is a satisfactory alternative treatment Dressings should not be done more frequently than once daily and small sores may be strapped and left much longer In the large chronic ulcers skin grafting is indicated to reduce the time of healing Septic complications such as cellulitis call for the usual treatment and oral sulphonamides or penicillin are indicated when there is evidence that streptococcal infection is spreading to surrounding tissues or lymph glands Diphtheritic sores are a special problem Skin grafting combined with large doses of penicillin and diphtheria antitoxin parenterally produce the best results

TROPICAL ULCER

Synonyms —Ulcus tropicum Naga sore Phagedenic ulcer, Tropical sloughing phagedena

Definition —Tropical ulcer is a gangrenous sloughing ulceration of the skin and subcutaneous tissues which may inolve underlying muscle tendons or bones it generally occurs in the humid tropics runs an intractable chronic course, fusiform bacilli and spirochætes are frequently demonstrable in the discharges

Ætiology —In contradistinction to desert sore this disease is generally, but by no means always confined to the damp steamy tropical jungles occurring most often within latitudes of 35 N 10° S It is common in underfed debilitated and diseased populations may affect people of any age and either sex, and occasionally assumes epidemic proportions especially amongst coolies or native labourers on the plantations and native tribes who eat a vegetarian diet containing only protein of low nutritional value Meat and fish eating tribes are rarely affected and outbreaks among the Somalis occur when the supply of camel s milk is low Some have regarded deficiencies in vitamin D, calcium nicotinic acid and riboflavine as factors in its development All agree that skin trauma is essential and that malnutrition and lack of personal cleanliness predispose to the condition

F fusiformis and spirochætes are commonly demonstrable in the ulcer (70 per cent) and less frequently staphylococci streptococci and bacilli of various types The condition is directly transmissible by inoculation of ulcer pus from man to man or the direct application of pus to the scarified skin over the external malleolus it is also recorded following the direct inoculation of anærobic cultures of *F fusiformis* into a traumatised area of dermis Though the ætiology remains doubtful the available evidence indicates *F fusiformis* is the probable cause

Pathology —There is coagulation necrosis and sloughing of the skin and subcutaneous tissue and separation of the slough leaves a foul acute ulcer with an adherent yellow base Vascular changes are said to occur even early in the disease and to consist essentially of thickening and narrowing of the lumina of vessels which may sometimes be obliterated and sometimes recanalised arteries veins and capillaries are all to some extent implicated (Golden and Padilla)

Symptoms —Phagedenic ulcers generally occur on the dorsum of the foot and the lower two thirds of the front of the legs The thighs the hands and forearms are rarely affected Ulcers are generally single but may be multiple and old scars indicating previous lesions may be present

The disease originates as a sero sanguineous bleb which soon ruptures leaving a dirty grey slough This process rapidly extends forming a foul sloughing ulcer with granulation tissue sides and adherent yellowish grey base which may attain several inches in diameter and gives rise to considerable pain and perhaps intermittent

where it caused considerable loss of manpower Laboratory and field investigations then indicated that the sores were due to infection of the skin following minor injury such as scratches abrasions and insect bites on exposed parts of the body The infecting agent was almost invariably a hæmolytic streptococcus often associated with a pyogenic staphylococcus (Keogh *et al*) In one or two minor outbreaks virulent diphtheria bacilli were isolated, but this finding is infrequent the cutaneous infection probably originated from latent or patent faucial or nasal diphtheria in the first instance Nor was there any discoverable relationship between these sores and deficiency of vitamin C in the rations, or latent scurvy as measured by urinary excretion tests The origin and persistence of these sores were largely connected with the difficulty of keeping the skin clean in a hot and dusty climate when arduous physical work had to be performed and little opportunity existed for bathing washing clothing or sterilising blankets Often the troops were crowded together under conditions when droplet spray infection of clothing and skin would occur some 7 per cent of troops harboured in their throats the same serological types of hæmolytic streptococcus as were isolated from the sores

Symptoms—The desert sore commences as a small vesicle or group of vesicles *containing clear fluid which soon becomes turbid and yellow* The lesions are situated on the dorsum of the hand and forearm and elbow when sleeveless shirts are used or the sleeves rolled up, around the knees and on the thighs when shorts are worn and they also occur on the dorsum of the feet the ankles legs and face The vesicles which are painful and surrounded by a dull red erythematous zone soon rupture and a circular or oval punched out ulcer is formed Its base, which is composed of granulation tissue exuding yellowish green pus is often covered by dark grey pseudo membrane which rapidly re forms if separated The edges are dull red at first but later bluish in colour In some instances undermining occurs and the ulceration may rapidly extend into fresh tissue at a time when the ulcer appears to be healing satisfactorily Desert sores are generally multiple they may cause considerable pain and lead to deterioration in general health especially if septic complications ensue They may take months to heal and often leave a thin scar Septic complications include cellulitis lymphangitis, adenitis bursitis and septicæmia

In those comparatively rare outbreaks in which true virulent diphtheria bacilli are demonstrable in the local lesions faucial diphtheria and carriers are generally prevalent and the cutaneous diphtheria has probably originated from droplet spray *infection of traumatised skin Diphtheritic palsies* such as paralysis involving the palate arms legs iris and muscles of accommodation were recorded in the War of 1914–1918 In campaigns in Palestine and the Western Desert a few such cases were encountered in the War of 1939–1945 but it was always doubtful whether the exotoxin causing such paralyses had been derived from the cutaneous membrane or from coexisting unsuspected faucial or nasal lesions

Treatment—PROPHYLACTIC—Efficient prophylaxis depends on prevention of *skin infection by personal hygiene and adequate first* aid treatment of minor skin traumata Bathing or a bath or shower after the day s work adequate changes of well washed clothing and sterilisation of sheets and blankets are important The surrounding skin area should be shaved the wound epilated and washed with a disinfectant soap or 2 per cent freshly prepared lysol solution followed by methylated spirits or iodine Elastoplast should then be applied and left *in situ* some 4 to 7 days

CURATIVE—*If seen in* the vesicular stage the vesicle should be pricked with a sterile needle the raised skin cut away hairs in the sore removed and a *moist eusol* dressing or diluted ammoniated mercury ointment applied Ambulatory patients who have resisted treatment those with multiple deep ulcers or sores around the ankle elbow and knee joint where movement prevents healing and those in which septic complications have ensued should be admitted to hospital for treatment. *Rest is an im*portant factor in the recovery of such patients and splinting may be necessary if multiple

(1) *Tinea cruris* or dhobie s itch (2) Hong Kong foot or ringworm of the foot (3) *T unguium* (4) *T imbricata* The first two are due to the *Trichophyton Epidermophyton inguinale* they are not peculiar to warm climates and are described elsewhere (pp 1236 1237)

TINEA UNGUIUM —A mycotic infection of the nails affecting Europeans from the Far East it may last for years and be associated with ringworm elsewhere The nail bed is involved leading to brittleness ridging and opaqueness of the nail Diagnosis is made by demonstrating *Epidermophyton inguinale* in scrapings mounted in liquor potassæ The application of a 2 per cent watery solution of copper sulphate or treatment with X rays may prove helpful In severe cases the nails may have to be removed before cure is effected

TINEA IMBRICATA (Tokelau) —A form of ringworm mainly indigenous in the Eastern Archipelago and South Pacific and characterised by non inflammatory raised brown spots giving rise to flaky tissue paper scales which are free centrally but attached at their peripheral bases producing a rosette like appearance These circles are about ½ in in diameter and as adjacent ones form they cause a characteristic festooned appearance The fungus *Endodermophyton concentricum* is readily demonstrable in the scales it affects the face, trunk and limbs but the palms soles scalp axillæ and crutch generally escape

The local application of linimentum iodide (B P) chrysarobin ointment (2 per cent) or of resorcin (1 drachm) in tinct benzoin co (1 oz) are curative Clothing should be boiled to prevent reinfection

PITYRIASIS VERSICOLOR or Tinea Flava is common in the tropics producing pale yellowish brown scurfy patches on the pigmented negroid skin especially on the face neck arms and chest Castellani holds that the yellow patches met with in his Ceylon cases differed from the brownish patches long recognised as being caused by *Microsporon furfur* in the European disease and has named the tropical variety Tinea flava and the causal fungus *Malassezia tropica* the black variety which is caused by *Cladosporium mansoni* Castellani calls Tinea nigra

The skin should be washed daily with green soap in spirit followed by the application of a saturated aqueous solution of sodium thiosulphate In severe cases ung hydrarg ammon dil should be applied daily Sterilisation of the clothing is necessary to prevent reinfection

PINTA

Synonyms —Mal de los pintos Caraate

Definition —A skin disease characterised by pigmentation depigmentation and hyperkeratosis caused by the *Treponema carateum*

Ætiology —The disease is found in tropical America and is specially common in Mexico and Colombia It occurs almost exclusively in dark skinned races and is caused by the spirochæte *T carateum* which morphologically resembles *T pallidum* and is demonstrable in the lesions Syphilis however does not appear to confer immunity Transmission probably occurs by direct contact or through flies feeding on open sores

Pathology —So far visceral lesions have not been described In the skin there are mild chronic inflammatory changes with disturbances of the melanophores and thickening of the corium Sections of the early lesions have revealed *T carateum* in the epidermis

Symptoms —The first stage is said to consist of a papule followed by a secondary stage when flat erythematous lesions known as pintids appear The late or tertiary stage is characterised by patches of pigmentation mainly involving the back of the hands and wrists or the feet and ankles and spreading to other parts of the body

fever, toxæmia and anæmia Sometimes there is spreading gangrene, and the ulcerative process involves surrounding or deeper structures like the toe nails muscles blood vessels, nerves and especially periosteum bone and joints Epidemics are recorded in which extension to tendons and bones occur in one third of the cases Three stages are recognisable (1) spreading sloughing ulceration (2) a stage of tissue equilibrium when destruction and growth of granulation tissue are equalised and (3) healing Often these ulcers persist for months unless properly treated one factor delaying healing is inadequate epithelial proliferation even after a healthy granulation tissue base has formed Excessive fibrosis and adhesion of scar tissue to bone is another cause of failure

Prognosis—Ulcers generally heal with modern treatment but the time taken varies with the facilities available for treatment the size and condition of the ulcer and the resistance of the patient In acute fulminating cases unless penicillin be available death may occur from toxæmia or septicæmia and amputation may be necessary to save life

Treatment—PREVENTIVE—In Europeans protection of the legs with gaiters or puttees is advisable in jungle countries and shorts should not be worn First aid treatment of minor skin traumata is essential A well balanced diet would probably prevent epidemics developing in native populations

CURATIVE—Continuous rest in bed is desirable but is frequently not practicable with natives the leg may have to be tied to some fixed apparatus to enforce this A well balanced nutritious diet adequate in high class protein and vitamins should be given any existent vitamin deficiency should be treated Cod liver oil calcium and certain vitamins of the B_2 complex have been specifically advocated

In the rapidly ulcerating stage complete debridement is an essential preliminary to any treatment Sloughs should be removed and the ulcer irrigated—preferably by diluted hydrogen peroxide Various treatments have been advocated Antiseptics such as carbolic copper sulphate eusol and proflavine have been widely used in the past a paint consisting of copper sulphate 2 drachms phenol 1 drachm glycerin 1 oz has proved useful Others prefer the application of hypertonic or isotonic magnesium sulphate to clean the ulcer Alternative treatments which have the advantage of avoiding daily dressings are to apply Z I P P to the ulcer and then put the leg up in a plaster cast (Cornell and Buchanan) or to firmly bandage with Elastoplast after dusting with iodoform powder Should septic dermatitis develop other treatment must be substituted without delay

The most promising of all recent treatments is penicillin In Europeans and in acute fulminating cases this should be given intramuscularly in appropriate dosage but this routine is generally not feasible in natives both on account of expense and because they object to multiple injections Excellent results have been reported with local penicillin applied as a powder in solution on gauze dressings or as a cream It should be continued for 2 or 3 days after fusiform bacilli and spirochætes have disappeared and the ulcer has become clean Oral chlortetracycline and chloramphenicol have recently been used successfully especially in early lesions which heal rapidly under such treatment and do not frequently relapse *Chlortetracycline* 500 mg 3 times a day for 2 to 10 days *Chloramphenicol* same dosage for 7 days

Whatever the treatment once the ulcer has become clean skin grafting including ' pinch grafts accelerate recovery In chronic ulcers where there is much fibrosis and the ulcer base has become adherent complete excision followed by skin grafting may be necessary

TINEA

Ringworm infections abound in the tropics, some being confined to special regions while others are much the same as in temperate climates The chief ones are

section of the nodules situated at the edge of the sore shows infiltration with plasma and round cells containing poorly staining nuclei in which phagocytosed bacilli may occur in clumps The granulomatous tissue is very vascular while in the older areas fibrosis and scarring are marked Spread is by direct continuity and the lymphatic system is never involved

Symptoms —The disease begins on the genitals as a flat papule which desquamates leaving a red granulation tissue surface which bleeds easily this superficial ulceration extends serpiginously producing offensive pus As the process advances the older areas cicatrise but this scar tissue readily breaks down again The disease is auto inoculable so that adjacent parts such as the scrotum and thighs or the surfaces of the labia become infected Ultimately the whole of the penis scrotum and groins *in the male* and the clitoris vulva labia vagina perineal and perianal region in women become involved and if unchecked the urethra and rectum as well Though skin ulceration extends slowly over a period of many years the process accelerates once the mucous membranes are involved and here there is little tendency to heal Until the terminal phase the general health remains good and the local lesions give rise to a minimum of pain and discomfort

Complications —These include recto vaginal fistula urethral stricture septic cystitis and pyelitis The lymph glands are only implicated if there is secondary coccal infection Cicatrisation may block the lymphatics and cause pseudo elephantiasis of the genitals

Diagnosis —Ulcerations due to syphilis tubercle or lupus vulgaris may be confused and where the glans penis is involved with fungating granuloma epithelioma may be suspected

Prognosis —This has greatly improved by modern treatment formerly the condition was hopeless frequently lasting for life

Treatment.—PREVENTIVE —As the disease is generally contracted by illicit intercourse with native women this should be avoided or appropriate prophylactic measures taken

CURATIVE.—Formerly the trivalent antimony compounds like tartar emetic Anthiomaline and stibophen (Fouadin) were widely employed and regarded as specifics Intravenous injections of tartar emetic were administered as in schistosomiasis (p 321) only a longer course of injections and a greater total dosage was given *i e* gr 50 to 150 Streptomycin chlortetracycline and chloramphenicol have proved considerably more satisfactory than antimonials in treatment Most cases even those resistant to antimony respond to these antibiotics and surgical excision and skin grafting should not be necessary *Streptomycin* 1 0 g intramuscularly every 6 hours for 5 days will cure most cases Pain is relieved in 24 to 48 hours in most cases and healing takes place within 4 weeks Relapses after streptomycin therapy are few and will usually respond to further treatment with this antibiotic, or to chlortetracycline or chloramphenicol *Chlortetracycline* 250 mg orally every 6 hours may be given until healing is complete A total dosage of 15 to 20 g is usually required *Chloramphenicol* up to 3 0 g orally per day may be given in divided doses Dosage for 10 to 12 days is usually adequate

BRIAN MAEGRAITH

The patches are generally symmetrical rough, dry and raised they vary in colour and progress finally to leucoderma Hyperkeratosis also is liable to involve the palms and soles There may be considerable itchiness and, if fissuring occurs an offensive serous discharge is liable to result The Wassermann and Kahn reactions are generally positive in the later stages of the disease

Treatment —The treatment is similar to that of syphilis neo salvarsan and similar arsenical drugs being specifics

PIEDRA

Piedra or trichosporosis is a disease common in Columbia and British Guinea in which hard gritty, black nodosities form around the hair of the scalp it is caused by the *Trichosporon giganteum* and may be confused with ordinary Trichomycosis nodosa

CREEPING ERUPTION

Synonyms —Larva migrans, Myiasis linearis, Hautmaulwarf

Definition —A peculiar linear slightly raised red eruption gradually creeping forward in a sinuous or straight line the posterior end fading away

Ætiology —The condition may be produced by *Gastrophilus* or other fly larvæ wandering under the skin but more commonly it is due to filariform larvæ of the cat and dog hookworm, *Ankylostoma braziliense* which have accidentally invaded man

Symptoms —The symptoms vary in different individuals and include smarting pain and intense itching along the raised line which first shows red spots and later hard round red papules 2 to 5 mm in diameter vesiculation or pustulation may occur Unless treated the condition persists for a long time

Treatment —Freezing the anterior end of the line where the larva is located with an ethyl chloride spray for 2 minutes is suitable for the type due to canine ankylostomes Oleum chenopodii applied locally either pure or diluted with 3 parts of castor oil has been favourably reported on If the lesions are produced by fly larvæ the skin should be dried cleaned with alcohol and cleared with cedar wood oil By means of a hand lens the larva can be seen as a spherical white mass at the end of its burrow Novocaine should be applied before local cauterisation

ULCERATING GRANULOMA

Synonyms —Granuloma venereum, Granuloma inguinale Granuloma inguinale tropicum, Ulcerating Granuloma of the Pudenda Serpiginous Ulceration of the Genitals

Definition —A very chronic ulcerating condition of uncertain ætiology occurring in the tropics involving the genitals perineum and groins

Ætiology —The disease occurs in the West Indies Guiana Brazil Puerto Rico parts of India and Africa the Pacific Islands and Northern Australia Both sexes are affected but not before puberty and all races are susceptible Donovan and many other observers have found a short oval bacillus specially located within the mononuclear cells it is a non motile capsulated bacterium of the rhinoscleroma group but though found with frequency in the lesions there is still doubt as to its real ætiological significance The disease itself is probably contracted during coitus

Pathology —The condition resembles an infective granuloma and microscopic

merely to an impairment of the sense of position—the function which those columns subserve—but also to a severe disturbance of the motor functions But the ataxia *which results is clearly produced by the activity of the intact motor structures working* in the absence of adequate sense of position and is an indirect or secondary effect of the lesion which is brought out only when the motor structures come into action

A final group of symptoms are those which we speak of as "*release phenomena*" When the coma of a hemiplegic patient has passed off he is left with paralytic symptoms namely the hemiplegia In a few weeks the paralysed limbs become spastic their tendon jerks increase and clonus makes its appearance These symptoms of persistent over action of intact nervous mechanisms freed by the lesion from the normal control of physiologically superior mechanisms are what are called release' symptoms Such symptoms may persist indefinitely and in some instances may entirely dominate the clinical picture

The symptoms produced by a lesion depend primarily on its localisation, *i e* on the nervous structures damaged by the lesion and from this aspect they are considered in some detail in a later portion of this section (p 1357) But it must be recognised that the symptoms may also be profoundly influenced by the pathological nature of the lesion A suddenly arising lesion such as an arterial occlusion or hæmorrhage or a direct injury is apt to produce a much more severe and definite local disorder of cerebral function than a slowly developing lesion of similar extent Indeed, it is often a matter of surprise to observe the degree to which the brain can adapt itself to structural changes which are brought about gradually Thus the intracranial cavity *may come to accommodate a large new growth which compresses and markedly* deforms the brain without giving rise to any objective symptoms or to any abnormal physical signs discernible on examination It is similarly known that a cerebral or cerebellar abscess is commonly present for some weeks before it reveals its presence by signs or symptoms this is its period of clinical latency

Again a tumour within the brain while it may give rise to symptoms of increased intracranial pressure such as headache vomiting and papillœdema may yield on examination few or no localising signs and this is not necessarily because it is in what is known as a silent area of the brain but simply because the essential nervous elements have not been seriously damaged by it For instance a glioma being a tumour of the interstitial elements may cause a minimal disturbance of observed nervous function even when large regions of the brain of known and specific function are directly involved by it

As another example of the modification of symptoms by the nature of the lesion a general disturbance may follow a local lesion as a result of what is known as *diaschisis* or *shock* We see this mode of disorder in the coma which accompanies a cerebral hæmorrhage In this state the cerebral hemispheres are for the time being out of action as a whole—even those parts not actually damaged by the lesion Such shock symptoms are necessarily transient

Finally we have to recognise that with space occupying lesions within the skull or brain there may ultimately arise indications of local disorder of function of parts of the brain remote from the lesion These may be spoken of as *false localising signs* and may result from such processes as œdema contre coup pressure or interference with the circulation of blood or cerebro spinal fluid

From what has been said it will be apparent that while the first step in neuro logical diagnosis is the recognition of the disorders of function present the localisa tion of a lesion (the topographical diagnosis) and the determination of its nature (the pathological diagnosis) are usually something *more than a simple essay in the* applied anatomy and physiology of the nervous system and that the complete diagnosis calls for a knowledge of the natural history of the different disease processes—that is of the pathology of nervous diseases—and for clinical experience

SECTION XVIII

DISEASES OF THE NERVOUS SYSTEM[1]

INTRODUCTION

THE diagnosis of a case of central nervous disease involves answers in turn to the two questions Where is the lesion? (the topographical diagnosis) and What is the lesion? (the pathological diagnosis)

Where is the lesion?—The central nervous system is not susceptible of examination by direct methods and all that can be examined are the functions of its various parts The first step is to determine as accurately as possible what disturbances of function are present (sometimes called physiological diagnosis) inferences can then be drawn as to what structures in the brain spinal cord or nerves are affected and consequently as to the site of a local lesion In occasional cases confirmatory localising information is obtained by special techniques such as radiographic examination and electro encephalography and in some cases these methods may even provide the only evidence of the location of the disease

What is the lesion?—In endeavouring to determine the nature of the disease present we are in general dependent on information obtained from sources other than the examination of the nervous system namely (1) the history of the case, (2) the general examination of the patient and (3) special tests

(1) In no department of medicine is careful and expert history taking more important The same physical sign has very different significance according to whether it has come on suddenly with moderate quickness or very gradually (2) A general examination of the patient should never be omitted Disease of the lungs heart blood vessels blood liver and abnormalities of the skin are all of great diagnostic significance in relation to nervous disease (3) Of the special tests ophthalmoscopic examination comes first and is always performed at the same time as the functional examination of the nervous system It often provides most important evidence of the nature of the disease The examination of the cerebro spinal fluid and the Wassermann reaction of the blood frequently help to reveal the kind of disorder present Radiographic examination its power now enlarged by special techniques may be equally diagnostic Electro encephalography is a relatively new aid, of which the diagnostic value is gradually increasing

Symptoms and their Modification—This brings us to a brief consideration of the ways in which lesions within the nervous system may disturb its functions The functions of a region of the brain that is directly involved in a disease process may be deranged in either of two ways They may be stimulated to over activity or they may be diminished or abolished We may thus speak of *irritative* or *excitatory symptoms* on the one hand and of '*paralytic symptoms* on the other a Jacksonian fit being an example of the first while hemiplegia is an instance of the second Thirdly impairment or abolition of one function may cause serious derangement of another A lesion of the posterior columns of the spinal cord gives rise not

[1] While this section has been largely rewritten the authors have made use of much of the material of previous editions and desire to express their indebtedness to the original authors The authors also thank Messrs Butterworth & Co (Publishers) Ltd for permission to make use of parts of Dr Purdon Martin's articl [illegible] rosyphilis in *The British Encyclopædia of Medical Practice*

merely to an impairment of the sense of position—the function which those columns subserve—but also to a severe disturbance of the motor functions But the ataxia which results is clearly produced by the activity of the intact motor structures working in the absence of adequate sense of position and is an indirect or secondary effect of the lesion which is brought out only when the motor structures come into action

A final group of symptoms are those which we speak of as "release phenomena' When the coma of a hemiplegic patient has passed off he is left with paralytic symp toms namely the hemiplegia In a few weeks the paralysed limbs become spastic their tendon jerks increase and clonus makes its appearance These symptoms of persistent over action of intact nervous mechanisms freed by the lesion from the normal control of physiologically superior mechanisms are what are called ' release symptoms Such symptoms may persist indefinitely and in some instances may entirely dominate the clinical picture

The symptoms produced by a lesion depend primarily on its localisation *i e* on the nervous structures damaged by the lesion and from this aspect they are considered in some detail in a later portion of this section (p 1357) But it must be recognised that the symptoms may also be profoundly influenced by the pathological nature of the lesion A suddenly arising lesion such as an arterial occlusion or hæmorrhage or a direct injury is apt to produce a much more severe and definite local disorder of cerebral function than a slowly developing lesion of similar extent Indeed it is often a matter of surprise to observe the degree to which the brain can adapt itself to structural changes which are brought about gradually Thus the intracranial cavity may come to accommodate a large new growth which compresses and markedly deforms the brain without giving rise to any objective symptoms or to any abnormal physical signs discernible on examination It is similarly known that a cerebral or cerebellar abscess is commonly present for some weeks before it reveals its presence by signs or symptoms this is its period of clinical latency

Again a tumour within the brain while it may give rise to symptoms of increased intracranial pressure such as headache vomiting and papillœdema may yield on examination few or no localising signs and this is not necessarily because it is in what is known as a silent area of the brain but simply because the essential nervous elements have not been seriously damaged by it For instance a glioma being a tumour of the interstitial elements may cause a minimal disturbance of observed nervous function even when large regions of the brain of known and specific function are directly involved by it

As another example of the modification of symptoms by the nature of the lesion a general disturbance may follow a local lesion as a result of what is known as *diaschisis* or *shock* We see this mode of disorder in the coma which accompanies a cerebral hæmorrhage In this state the cerebral hemispheres are for the time being out of action as a whole—even those parts not actually damaged by the lesion Such shock symptoms are necessarily transient

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DISORDERS OF THE CRANIAL NERVES

THE OLFACTORY NERVE AND TRACT

Small olfactory *nerve filaments arise from special receptors in the olfactory* portion of the nasal mucosa, and joining together into small nerves pass through the cribri form plate of the ethmoid bone to end in the two olfactory bulbs From each olfactory bulb an olfactory stalk passes backwards on the inferior *surface of the frontal lobe of* the brain and ends in two roots lateral and medial, on either side of the anterior perforated spot

Loss of the sense of smell (anosmia) is *frequently due to disease of the nasal* mucosa and only occasionally is it of diagnostic value in cases of nervous disease or injury It occurs in cases of head injury especially if the patient has fallen upon his forehead or upon his occiput and is usually due *to tearing of the olfactory nerves,* with or without fracture of the cribriform plate In most cases the loss of smell is permanent

Unilateral or bilateral anosmia may result *from meningeal* tumours arising from the olfactory groove and pressing on the inferior surface of one or both frontal lobes and it occasionally results from basal syphilitic meningitis

Flavours are actually appreciated by the sense of smell so that a patient who has lost this sense is apt to think that he has lost his sense of taste as well but if the sense of taste is retained he will still be able to appreciate the primary flavours—salt sweet, bitter and acid

THE OPTIC NERVE

The optic nerve is developed as a cerebral tract and retains something of that character throughout life The primary visual neurones are situated entirely in the retina it is the neurones of the second order whose fibres form the optic nerves and tracts *Disturbances of these structures are frequent and are of great importance* in many kinds of nervous disease

The optic nerve head or optic disk can be seen with the ophthalmoscope and is the only *part of the central nervous system which can be examined* by inspection Congenital abnormalities of the optic disk are not uncommon the most important being the presence of opaque nerve fibres When viewed with the ophthalmoscope a *bundle of opaque nerve fibres is seen* as a glistening white streaky mass appearing to stream out from the nerve head into the adjacent parts of the retina The fibres may be limited to one quadrant, or may be all round the disk The acquired disturb *ances of the optic nerve* give rise to four principal syndromes (1) papilloedema *(2) optic neuritis or neuro retinitis, (3)* retrobulbar *neuritis and (4) optic atrophy*

PAPILLŒDEMA

The term denotes an œdema of the optic papilla or nerve head, and the significance of such œdema lies in the fact that it is almost invariably due to raised intracranial pressure it is frequently the only objective sign of that state, and it is important that the student should be familiar with it in all its stages Before there is any actual œdema of the optic nerve head the principal veins of the retina may appear distended and the disk appears somewhat redder than its normal colour *Then the margin of* the disk becomes blurred in its upper and inner quadrant or in its uppermost portion this blurring extends around the disk and at the same time the cup of the disk becomes filled up The disk becomes *much redder* than normal and may be of almost the same colour as the retina The disk continues to swell and bulges slightly into the

eye and this swelling can be measured with the opthalmoscope relative to the surrounding retina in terms of dioptres a swelling of 4 dioptres is common but higher degrees of swelling are rare As the swelling increases the disk margins become still more blurred and some hæmorrhages and exudate may appear With the increase of swelling the arteries appear to sink down as they pass off the disc on to the retina and the retina close to the disk especially on the macular side may show some swelling or tendency to fold When the rise of intracranial pressure is slow the œdematous disk is less highly coloured than when the pressure rises quickly and the œdema is more acute In the early stages of papillœdema there is little disturbance of vision but when the swelling becomes severe the patient begins to complain of some blurring of vision and of transitory severe disturbance of sight (amaurosis fugax) associated with stooping or with physical effort

If the intracranial pressure is high and is not soon relieved the sight eventually fails the disk becomes paler and takes on a somewhat waxy appearance and gradually subsides into atrophy This consecutive ' or ' post neuritic atrophy can in many instances be recognised ophthalmoscopically by the irregularity of the edges of the atrophied disk consequent on the preceding swelling and exudation

OPTIC NEURITIS AND NEURO RETINITIS

Actual inflammation of the nerve head is rare but the abnormal state of the disk and retina that is associated with renal disease with arterial hypertension is often mistaken for papillœdema due to raised intracranial pressure The disc is blurred and usually slightly swollen the swelling of the disk however rarely exceeds 2 dioptres while the changes in the retina are pronounced and extensive and are much greater than those that may be associated with papillœdema

RETROBULBAR NEURITIS

This term is applied when disease regarded as inflammatory affects the optic nerve behind the papilla and as a rule the disease is situated farther back than the point about half an inch behind the eye where the central vein emerges from the optic nerve

Local lesions in the substance of the nerve between the globe of the eye and the chiasma are very common and according to their severity give rise to partial or complete blindness in the corresponding eye As the central part of the optic nerve is the site of election for such lesions the visual defect is commonly in the form of a central scotoma This is the characteristic disturbance and is usually acute or subacute in its onset but there are a number of associated phenomena The patient frequently complains of pain on movement of the eyeball and sometimes of pain above the eye The fundus of the eye usually looks normal but when the disease comes forward to the papilla redness of the optic disc and blurring of its edges may be apparent The pupil is usually moderately dilated, it reacts to light but often does not maintain the reaction These associated phenomena soon pass off and in most cases the central scotoma begins to diminish within a few weeks The prognosis depends however on the cause of the syndrome

Disseminated sclerosis is the usual cause of acute retrobulbar neuritis With this condition the disturbance is almost invariably unilateral and a great degree of recovery is the rule Functional recovery may be complete in other cases a central scotoma for colour or a small absolute central or paracentral scotoma is left Characteristically a slight degree of optic atrophy follows causing permanent pallor of the temporal half of the optic disc

Bilateral retrobulbar neuritis occurs from toxic causes and also occasionally without discoverable cause and the outlook for recovery of vision in such cases is

always doubtful The less severe toxic cases are usually due to tobacco, more severe disturbances are due to such causes as poisoning by wood spirit present in alcohol by arsenical compounds such as tryparsamide, by lead compounds and by quinine Retrobulbar neuritis may also be bilateral in neuro myelitis optica, a rare demyelinating disease closely resembling an acute form of disseminated sclerosis Leber's disease is a familial malady characterised by retrobulbar neuritis, males only are affected and the symptoms make their appearance after puberty and usually before the age of 25 Repeated attacks may occur and a severe degree of optic atrophy result

OPTIC ATROPHY

Optic atrophy is recognised on ophthalmoscopic examination, by a peculiar whiteness and flatness of the disk with a very high contrast at the edge of the disk between disk and surrounding retina both as regards colour and limitation The lamina cribrosa—the sieve like cross latticing of the strands of the sclerotic through which the bundles of optic nerve fibres pass—becomes visible as a stippling of the temporal region of the disk The vessels of the retina become atrophied, and are seen *to be unduly small* In many atrophies the edge of the disk is sharply cut but when atrophy follows papillœdema the edge is apt to be fluffy like that of torn cotton wool Optic atrophy is usually classified as primary or consecutive, according to whether the atrophy of the disk is the first observable change or follows upon papillœdema or inflammation of the disk or optic nerve

Ætiology—*Primary optic atrophy*—1 This is of frequent occurrence in the hereditary or congenitally installed diseases in which primary degeneration of neurones occurs and in particular it occurs in association with the hereditary ataxias In amaurotic family idiocy and retinitis pigmentosa, both of which are familial diseases optic atrophy is consequent upon degeneration of the neurones in the retina 2 It *is one of the common manifestations of syphilis of the nervous system* and may occur alone but much more usually it occurs as part of the syndrome of tabes or of general paralysis It is not uncommonly met with in congenital syphilis 3 It results from lesions of the optic chiasma and optic nerve and is the constant result of long continued pressure upon these structures This variety often called *retrograde optic atrophy* is usually due to pituitary and other tumours in the neighbourhood of the chiasma, and occasionally to tumours aneurysms or bony injuries behind or involving the optic foramen It also results from local disease within the orbit 4 It may follow the exhibition of certain drugs such as tryparsamide methyl (wood) alcohol, quinine 5 It may result from severe hæmorrhage from any part of the body or from anæmia and may occur in association with pernicious anæmia and subacute combined degeneration of the spinal cord Optic atrophy may also result from diabetes arterial disease (with or without thrombosis of the central artery of the retina) and from glaucoma

Consecutive optic atrophy—1 This follows the more severe grades of papillœdema and is due to strangling of the optic nerve fibres by the œdema in the first place and by the cicatrisation subsequently Severe degrees of papillœdema may if pressure be relieved recover perfectly without atrophy or impairment of sight 2 It follows inflammation of the optic nerve and in occasional cases is seen in the late stages of the neuro retinitis associated with arterial hypertension 3 Partial optic atrophy of varying degree is an almost constant result of retrobulbar neuritis

THE OCULO MOTOR NERVES

The third nerve supplies the internal muscles of the eye and all the external muscles of the eyeball with the exception of the superior oblique (which is supplied

by the fourth nerve) and the external rectus (which is supplied by the sixth nerve) Complete paralysis of the third nerve produces a dilated and inactive pupil complete ptosis and loss of upward downward and inward movements of the eye the eye assumes a position of downward and outward strabismus As a rule diplopia is not complained of because of the dropping of the lid Many third nerve palsies are, however partial, and the muscles innervated by the nerve may be affected in different degrees When diplopia is present it is a crossed diplopia because the strabismus is divergent there is secondary deviation of the sound eye and false projection in the visual field

The fourth nerve supplies the superior oblique muscle Paralysis produces no obvious strabismus but in looking outwards or downwards there is a wheel movement of the globe which can be detected by observing the conjunctival vessels when the eye moves The diplopia is most discomforting and occurs in every position of the eyes except on looking up The diplopia is uncrossed and the false image is lower than and with its top tilted toward the true image

The sixth nerve supplies the external rectus muscle Paralysis of it produces a convergent squint and uncrossed diplopia

These oculo motor nerves may be affected singly or in various combinations and the paralysis of any one of them may be complete or partial In some cases the lesion responsible for the paralysis lies within the brain stem where it may affect either the nuclei of the nerves or the nerve fibres in their intra cerebral course More often the lesion affects the nerve in its peripheral course—within the cranium in the neighbourhood of the sphenoidal fissure or within the orbit To attempt to give a list of all the possible lesions—inflammatory neoplastic hæmorrhagic or traumatic—that affect these nerves would serve no useful purpose but the following may be noted and certain syndromes should also be recognised Syphilis is a common cause of third nerve paralysis by involvement of the nerve in syphilitic meningitis less commonly the sixth and fourth nerves are affected by the same process Any of the forms of acute and subacute meningitis may similarly involve one or more of the oculo motor nerves Secondary malignant deposits in the meninges or in the brain stem are not uncommon causes of ocular palsies Primary intracranial tumours and aneurysms may cause paralysis of any or all of them by direct compression but intra cranial pressure of itself may cause paralysis of the sixth nerve as a result of downward displacement of the brain stem Paralyses of the sixth nerve are frequently rheumatic (i e of undetermined cause) or are associated with generalised arterial disease or with diabetes the mechanism of the paralyses in such cases is obscure but recovery within a month or two is the rule A variable ocular palsy or variable diplopia is often due to myasthenia gravis

Syndrome of the sphenoidal fissure —All the oculo motor nerves enter the orbit by the sphenoidal fissure and they are accompanied by the branches of the first division of the trigeminal nerve and the ophthalmic veins while the second division of the trigeminal nerve enters the infra orbital canal at the apex of the orbit All these structures may be involved by a lesion at the sphenoidal fissure the most common causes being aneurysm of the internal carotid artery at the anterior end of the cavernous sinus and meningeal tumour The syndrome usually begins with pain in the eye and forehead Soon afterwards some proptosis is evident and there is pain on pressing the globe backwards This is followed by signs of involvement of the oculo motor nerves The sixth is the first and sometimes the only nerve involved and usually its paralysis is followed by that of the fourth the first division of the fifth the third and sometimes the second division of the fifth in that order The final result may be a total ophthalmoplegia with anæsthesia of the eye corresponding half of the fore head and the cheek severe pain in the same distribution and unilateral proptosis but the syndrome is often incomplete When it is due to aneurysm the condition may largely recover within a few months

The oculo motor nerves may be paralysed in the *wall of the cavernous sinus* either as a result of thrombophlebitis of the sinus or of an aneurysm of the internal carotid artery

Gradenigo s syndrome —This consists of paralysis of the sixth nerve and pain of trigeminal distribution associated with middle ear disease It has been attributed to localised meningitis at the tip of the petrous bone but Symonds has pointed out that it may be due to thrombosis of the inferior petrosal sinus It is usually seen in children, and radical treatment of the ear disease is indicated

Lesions within the brain stem may produce combined oculo motor palsies, other cranial nerves may also be affected or the long projection paths may be involved Finally supra nuclear ocular palsies may arise, as described below Nuclear palsies may result from tumours disseminated sclerosis epidemic encephalitis tuberculoma and small peri aqueductal hæmorrhages The rare condition known as *chronic progressive external ophthalmoplegia* formerly ascribed to degeneration of the oculo motor nuclei is now believed to be due to myopathic disease of the muscles within the orbit This disease may begin in young subjects it is slowly progressive and leads to paralysis of all the external ocular muscles with ptosis which is usually incomplete the internal ocular muscles are unaffected

Oculo motor nerve fibres within the brain stem may be affected by vascular neoplastic and granulomatous lesions Thus a lesion in the cerebral peduncle will produce an ipsilateral third nerve paralysis with hemiplegia on the opposite side of the body (*Weber s syndrome*) and a lesion involving the red nucleus may cause an ipsilateral third nerve palsy with tremor of the limbs on the opposite side (*Benedikt s syndrome*)

CONJUGATE PARALYSIS

The uppermost portion of the main third nerve nucleus is concerned with upward movement of the eyes (superior recti) and the inferior recti are represented next in order from above downward Bilateral lesions involving the upper parts of both nuclei consequently bring about a loss of vertical movements of the eyes the horizontal movements being retained The lowest part of each third nucleus is concerned with the internal rectus muscle and is connected with and partly governed by the sixth nucleus of the opposite side A bilateral lesion at the level of the upper part of the pons by involving these structures may cause paralysis of horizontal movement of the eyes vertical movements remaining unaffected Paralysis of conjugate movements to one side occurs less frequently The power of convergence is sometimes preserved when conjugate horizontal movement is lost

SUPRA NUCLEAR OCULAR PALSIES

In some cases although the patient is unable voluntarily to perform certain ocular movements it can be demonstrated that the muscles and nerves concerned are not paralysed and movements of the eyes can be brought about reflexly by appropriate stimuli The paralysis is therefore supra nuclear and comparable to an upper motor neurone paralysis The patient may be unable to deviate his eyes to order but deviation may be produced by labyrinthine stimulation Or again the patient may be unable to follow a moving object with his eyes but if he fixes an object and his head is rotated passively his gaze may remain fixed on the object and his eyes thus take up a position of deviation In rare cases the eyes when the head is still may follow an object which the patient fixes intently The lesions concerned are believed to be situated in the brain stem close to the oculo motor nuclei

ABNORMALITIES OF THE PUPIL

Myosis or abnormal smallness of the pupil may be due to paralysis of the cervical sympathetic (p 1345) minute pupils are sometimes associated with syphilis of the

nervous system particularly tabes each pupil being possibly little larger than the head of a pin (spinal myosis) myosis occurs also with acute lesions of the pons and it may be met with in advanced age without pathological associations It is a well known sign of the action of morphine and it is produced also by the local action of eserine instilled into the eye

Mydriasis denotes dilatation of the pupil The sphincter pupillæ muscle is controlled by the small nucleus of Edinger Westphal which is the uppermost part of the third nerve nucleus Mydriasis may therefore, result from paralysis of the Edinger Westphal nucleus and more commonly it is one of the features of paralysis of the third nerve It results also from the action of belladonna or atropine—or of cocaine whether taken internally or used as eye drops

Inequality of the pupils has numerous causes Obviously it may result from any of the causes of unilateral myosis or of unilateral mydriasis given in the preceding paragraphs Less specifically it is common in nervous syphilis It may result from a blow on one eye or from disease of the eye It occurs as a transitory phenomenon after the prolonged use of one eye especially against a bright light as in using the microscope It is common with local cerebral lesions of all kinds including closed head injuries It is a feature of cases of intradural and of subdural hæmatoma

Irregularities of the shape of the pupil are less common than inequality of the pupils They may be due to local disease of the irides but in certain cases of disease of the brain stem especially syphilitic disease one or both pupils may be oval in outline without evidence of local disease of the irides Irregularity of the pupils is common in neuro syphilis generally and is frequently associated with atrophic changes in the irides, such as are associated with diabetes

ARGYLL ROBERTSON PUPIL

The normal pupil contracts briskly when light falls upon the eye and dilates in darkness it also contracts in association with accommodation and convergence The reaction to light is reflex and this reflex response to light may be lost when other reactions of the pupil are retained (reflex iridoplegia) In the particular form of reflex iridoplegia known as the *Argyll Robertson pupil* the pupil is abnormal in that (1) it does not react at all to light (2) it is very small and (3) it does not dilate fully under the influence of a mydriatic, while it is normal in that (1) it reacts normally with accommodation convergence also (2) reasonably good vision in the eye concerned is an essential part of the phenomenon Such a pupil is almost invariably due to syphilis of the central nervous system and is seen most frequently and characteristically in tabes dorsalis The phenomenon is ordinarily bilateral, but there are often differences in size between the two pupils and usually the pupils are irregular in outline Atrophic changes in the irides are generally apparent

The afferent fibres of the light reflex arc pass back with the visual fibres in the optic nerve and optic tracts but whereas the visual fibres end in the lateral geniculate body the fibres which serve the light reflex pass on to enter the superior corpus quadrigeminum From there a connection is formed by another fibre with the upper part of the oculo motor nucleus (Edinger Westphal nucleus) The efferent fibres of the reflex arc form part of the oculo motor nerve Since with the Argyll Robertson phenomenon vision is good the visual path is evidently intact and since the pupil contracts with accommodation convergence the cells and fibres of the third cranial nerve which innervate contraction of the pupil must be intact the arc must therefore be interrupted in its middle portion *i e* between the place where the light reflex fibres leave the visual fibres and the oculo motor nucleus Degeneration of the fibres forming this middle portion of the arc is not however easy to recognise by staining methods and this theory still awaits anatomical confirmation

The Argyll Robertson pupil once established persists in spite of antisyphilitic

treatment As the tabetic process advances the accommodation convergence reaction may gradually be lost and the pupil thus ceases to show the dissociation of reactions typical of the Argyll Robertson phenomenon and becomes a fixed pupil

Modifications of the Argyll Robertson pupil are frequently encountered in diseases of the nervous system A slight reaction to light may be present in a pupil which otherwise conforms to Argyll Robertson s description This represents a preliminary stage of the complete phenomenon and its significance is similar

More frequently the pupil reacts normally with convergence and does not react to light but it is not small and may even be dilated Such a pupil is common in central nervous syphilis but has not the diagnostic significance of the complete Argyll Robertson phenomenon *for it may be due to any lesion interrupting the light* reflex arc in its middle portion A pineal tumour for instance or a tuberculoma or a patch of disseminated sclerosis may cause this abnormality and it has been described in association with many different nervous diseases If however atrophic changes are present in the iris the condition is likely to be syphilitic

PSEUDO ARGYLL ROBERTSON OR MYOTONIC PUPIL

Pseudo Argyll Robertson pupil (Foster Moore) or myotonic pupil (Adie) is a non syphilitic abnormal condition of the pupil in which the reactions are all slow *but the light reaction much slower than the convergence reaction The pupil is of* ordinary size or somewhat larger and is usually bigger than the unaffected pupil of the other eye No reaction is obtained to the light of a torch shone on the eye but if the patient sits for 10 or 15 minutes in a bright diffuse light the pupil gradually contracts and if he sits in a dark room it dilates slowly During accommodation convergence contraction of the pupil takes place slowly and continues through an abnormal range of movement so that as convergence is maintained the myotonic pupil finally becomes smaller than its fellow After relaxation of convergence the pupil takes many minutes to dilate to its former size In pupils of this kind prompt and full dilatation occurs with mydriatics

The phenomenon is usually *unilateral and the iris of the affected eye* does not show degenerative changes such as usually accompany the true Argyll Robertson pupil Accommodation may be involved in the disturbance and then the patient complains of inability to focus with the affected eye

Ætiology—The cause of this phenomenon is unknown It is the more likely to be mistaken for a syphilitic abnormality because in some cases it is associated with absence of some of the tendon jerks in the limbs Once established it persists but as far as is known at present it is not associated with any progressive disease

The difference between the true and pseudo Argyll Robertson pupils may be tabulated as follows

TRUE ARGYLL ROBERTSON PUPIL	PSEUDO ARGYLL ROBERTSON PUPIL
Quite inactive to light or darkness	Reacts slowly to light and darkness
Reacts briskly *with convergence*	*Reacts slowly* with convergence
Smaller than normal	Larger than normal
Ordinarily bilateral	Usually unilateral
Usually irregular in outline	Regular in outline
Iris shows atrophic changes	Iris looks healthy
Dilates imperfectly with mydriatics	Dilates fully with mydriatics

PARALYSIS OF THE REACTION WITH ACCOMMODATION

The pupil does not contract when an effort to accommodate is made Accommodation itself may or may not be present *i e* the ciliary muscle may or may not

be acting This condition is most commonly seen as an after effect of encephalitis lethargica, and so is usually associated with the post encephalitic Parkinsonian state

Conversely the ciliary muscle may be paralysed and the patient be deprived of accommodation but the pupil may still contract in association with the effort to accommodate This occurs in diphtheritic paralysis of which it is one of the earliest symptoms and it is said to occur sometimes in tabes It must depend on disease of the centres in the nuclei of the third nerves

In cases of disease of the third nerve the ciliary muscle is paralysed as well as the iris

PARALYSIS OF THE CERVICAL SYMPATHETIC

Synonym —Horner s Syndrome

So far as the eye and orbit are concerned the sympathetic is the tonic retractor of the lid the tonic protruder of the eyeball and the tonic dilator of the pupil and stimulation of this mechanism results in retraction of the lids or widening of the palpebral fissure exophthalmos and wide pupil while paralysis of the cervical sympathetic produces narrowing of the palpebral fissure (cervical sympathetic ptosis) and a small pupil It is customary to include enophthalmos amongst components of cervical sympathetic palsy but in many cases this is not recognisable The excitation is seen in Graves disease the paralytic condition is of common occurrence in nervous diseases The cervical sympathetic is also the tonic vaso constrictor and secreto motor nerve of the head generally but disturbance of this mechanism does not often give rise to characteristic, or important clinical phenomena A curious lack of expression is however sometimes observable in the face on the side of the lesion Cervical sympathetic paralysis occurs in the following clinical associations (1) In many lesions of the brain stem or of the cervical portion of the spinal cord especially when the last cervical and first dorsal segments or roots are damaged It is common in syringomyelia (2) In lesions of the cervical sympathetic trunk by trauma pressure growths etc. (3) It is very common in tabes and nervous syphilis generally where it appears as partial bilateral ptosis with small pupils It appears to be due to a primary neuronic degeneration in this condition and never improves

THE FIFTH OR TRIGEMINAL NERVE

The fifth nerve arises from the pons by a large sensory and a smaller motor portion The sensory portion supplies sensation of all forms to the same side of the face and anterior half of the scalp Its ganglion cells lie in the Gasserian ganglion, which lies *near the apex of the petrous bone and distal to the ganglion the nerve* is in three divisions (from which the nerve derives its name) The first or ophthalmic division passes forward on the wall of the cavernous sinus and enters the orbit in three branches It supplies sensation to the forehead and anterior portion of the scalp to the eye and to the ridge of the nose The second or maxillary division leaves the cranium by the foramen rotundum passes across the spheno palatine fossa and enters the infra orbital canal Having traversed the canal it emerges on the anterior surface of the maxilla half an inch below the lower rim of the orbit and its branches spread out to supply the skin of the cheek and upper lip the mucous membrane of the nose the upper jaw and the hard and mo t of the soft palates The third or mandibular division leaves the cranium through the foramen ovale and enters the infra temporal fossa it is accompanied by the motor root which here unites with it to form a single trunk It supplies sensation to the skin of the lower lip

chin and outer part of the cheek and by its auriculo temporal branch to part of the auricle and to the temporal area it also supplies the mucous membrane of the lower lip lower jaw floor and sides of the mouth and anterior two thirds of the tongue Its lingual branch contains taste fibres from the anterior two thirds of the tongue which however leave it by the chorda tympani nerve and pass over to the facial nerve The motor root of the trigeminal nerve innervates the temporal muscle masseter buccinator, internal and external pterygoids mylo hyoid anterior belly of the digastric and also the tensor tympani and tensor velipalatini

The fifth nerve may be involved in the pons by tumours and not infrequently by disseminated sclerosis the Gasserian ganglion may be irritated or compressed by tumour or aneurysm and it is frequently the site of herpetic inflammation with a consequent herpetic eruption over the area of the external distribution of the nerve most commonly only the ophthalmic division is thus affected (see Herpes Ophthalmicus) Organic lesions of the divisions of the nerve or their branches at first cause pain and then sensory loss with a distribution corresponding to the portion of the nerve involved Loss of the corneal reflex is often the first indication of involvement of the fifth nerve *e g* in cases of acoustic nerve tumour

Paralysis of the motor function of the fifth nerve occurs in lesions of the nucleus in the pons or of any part of the peripheral course of the motor division The signs of such paralysis are not apparent to the patient who experiences no difficulty in mastication provided the lesion be unilateral To the observer the jaw deviates to the side of the paralysis when the mouth is opened on account of the action of the unopposed external pterygoid of the sound side The masseter, as felt by the finger on its anterior edge does not harden on biting nor do the temporal muscles harden and wasting of these muscles may be evident The floor of the mouth does not stiffen on the paralysed side when the mouth is forcibly opened

Bilateral involvement of all the muscles supplied by the fifth nerve is the rule in all cases of progressive muscular atrophy when the bulbar nuclei are affected

TRIGEMINAL NEURALGIA

Synonym —Tic Douloureux

Definition —A malady characterised by paroxysms of intense pain of a sharp stabbing nature within the distribution of the trigeminal nerve without sensory loss or other evidence of organic disease of the nerve

Ætiology —The cause of trigeminal neuralgia in most cases is unknown The vast majority of patients are over 50 years of age and most of them are arteriosclerotic and have high blood pressure Females are affected more frequently than males A number of cases in younger people are due to disseminated sclerosis and there is also a form different from the chronic trigeminal neuralgia of elderly people which occurs temporarily in young subjects from exposure to cold and may recur

Symptoms —The chief feature of the malady is pain which may be general throughout the area of distribution of the nerve but which is more commonly confined to one of the three divisions of the nerve and often to one branch of a division It is characteristic for the pain of neuralgia to commence locally and subsequently to spread in each attack and gradually in the course of the disease permanently to invade a larger area Two different kinds of pain occur the sharp and paroxysmal and the dull continuous pain The paroxysmal pains are sudden in onset and in cessation They have a lightning like character and are described as piercing knife like or as if the affected region were penetrated by red hot wires

Though often quite spontaneous these pains may be brought on by movements of the face and jaw or by touching the surface or by a cold wind The sufferers typically describe them as brought on by eating and talking and washing the face and may wear a scarf round the head to protect the affected side of the face from the

wind Mastication may become so difficult as to render the feeding of the patient a matter of anxiety The paroxysms are brief seldom lasting longer than 1 or 2 minutes but they may recur frequently, and the patients usually describe different degrees of liability to them at different times

When the paroxysms are occurring in a severe case the patient remains for a period which may be from a few minutes to several hours paralysed under the fear of pain unable to move a muscle lest a spasm more dreadful than the last should occur The paroxysmal pains are usually followed if severe by a more lasting dull continuous pain often of a boring character and sometimes such pain becomes absolutely continuous The skin over the affected region is sore and tender after the paroxysm and the patient may be unable to bear brushing the hair or shaving the face The pain may be of every degree of severity from mild momentary starts to continuous incapacitating pain interrupted only by excruciating attacks of agony which render life a burden

The distribution of the pain is usually in one or two divisions of the nerve The first division is rarely affected primarily but pain may spread into it from the second division If the pain begins in the second division it may after a time affect the third and vice versa The lightning like onset of the agony often causes convulsive spasm of the face and of the body and limbs The tender points of Valleix or trigger zones are constantly present during the attack and for some time afterwards When the second division is affected a little œdema develops under the orbit when paroxysms are frequent When the third division is affected unilateral furring of the tongue occurs Fortunately the attacks usually cease at night

Diagnosis—The quality of the pain is characteristic and when trigeminal neuralgia is present the diagnosis is not often missed especially if a paroxysm is witnessed The usual mistake is to regard as trigeminal neuralgia pain that is due to some other cause and since there are very many conditions that give rise to pain in the face the opportunities for error are numerous Unless the pain is brought on by eating and talking and washing the face it is almost certainly not due to trigeminal neuralgia Pain that is constant or of a continuous character is not due to trigeminal neuralgia and some other cause should be sought Disease of the frontal sinus and glaucoma should be kept in mind Local painful neuro es or psychogenic pains are continuous though subject to fluctuation and when at their worst they often spread to the other side of the face as trigeminal neuralgia never does

A similar neuralgia occurs in the glosso pharyngeal nerve but is much rarer the pain is induced by the movement of swallowing and is felt in the ear or throat

Course—In the early stages remissions lasting months or years are usual but in old patients remissions if they occur are likely to be brief In all cases the remissions become shorter as time goes on and unless the affected division of the nerve is destroyed the neuralgia persists for the rest of the patient s life In occasional cases the disease is bilateral

Treatment—In the first place it is essential to make sure that all possible causes of local irritation in the region of distribution of the fifth nerve are absent or if present adequately dealt with Secondly it is important to remember that in its early stages the malady shows complete remissions of long duration These remissions do indeed tend to become shorter after some years but their occurrence suggests that in planning treatment it is essential to consider the circumstances of each individual case Thus if a patient who may be expected to enjoy a long period of freedom from pain can be tided over the present attack by medical means it is clearly not wise to give an alcohol injection immediately

In the hope that remission will occur medicinal treatment should be given a trial provided the pain is not too intense Tinct gelsemii in doses of 10 to 20 minims is an old fashioned and seemingly effective remedy and may be combined with

phenazone gr 10 in solution or aspirin gr 10 in emulsion and with liq arsen min 2 This should be taken regularly three or four times daily when the attacks of pain are prevalent and the number of doses may be reduced when the frequency of pains diminishes

If after a few weeks of such treatment the neuralgia is still severe more effective measures should be employed without delay One affected branch of the nerve may be destroyed temporarily by injection of alcohol into it the corresponding area of the face being thereby rendered anæsthetic The permanence of the relief obtained by a successful peripheral injection varies and is usually longer when the third division is concerned than when the second is the affected one The operation is at all times a tricky one requiring great skill on the part of the operator, and subsequent injections become more and more difficult Alternatively the Gasserian ganglion can in most patients be injected with alcohol but while this gives a permanent result it has the disadvantage that the whole of the affected side of the face is rendered completely anæsthetic including of course the eye in which severe trophic keratitis will quickly develop unless adequate precautions against its occurrence are taken at the time of the injection However injection of the ganglion is an excellent treatment in skilled hands In general the most successful treatment is operative sub total division of the sensory root of the fifth nerve proximal to the Gasserian ganglion This renders the area of the second and third divisions anæsthetic and allows sensation to be retained over most of the area of the first division thus avoiding risk to the eye and the effect of the operation is permanent The practice of different physicians in recommending this operation varies considerably but it has been performed successfully on patients of all ages and the mortality nowadays is low In the case of a patient under the age of 50 years in whom the neuralgia seems established operation should be advised at once since the patient may still have many years of life before him and the neuralgia will never leave him for more than a few months With older patients each case must be considered on its merits

The operation of stripping the dura from the Gasserian ganglion and its immediate vicinity is under trial and has given good results over a short period

THE SEVENTH OR FACIAL NERVE

The seventh nerve supplies all the muscles of the face the platysma and the muscles of the scalp It is a purely motor nerve but the taste fibres which convey taste from the anterior two thirds of the tongue join it by way of the chorda tympani nerve and are incorporated in it for part of its course Fibres which excite salivary secretion are also associated with it at one part

The facial nerve may be paralysed in cases of pontine tumour or hæmorrhage, or in association with tumours or syphilitic meningitis in the cerebello pontine angle or by inflammation or operative intervention in the middle ear it may be paralysed within the facial canal as a result of herpes of the geniculate ganglion inflammation or compression of the nerve within the stylomastoid foramen is the cause of the common Bell s palsy and enlarged glands behind the angle of the jaw or a tumour of the parotid gland or traumatic lesions may be responsible for paralysis of the nerve just before it divides into the branches which distribute it over the face Bilateral facial paralysis not infrequently occurs in acute infective polyneuritis

Paralysis of the face due to a lesion of the facial nerve or its nucleus causes as a rule equal paralysis or uniform weakness of all portions of the affected half of the face If the lesion is in the pons the sixth nerve is usually affected as well When the lesion is at the internal auditory meatus or in the middle ear or at the geniculate ganglion the taste fibres are involved and taste is lost on the anterior two thirds of the tongue on the affected side

1 BELL S PALSY

Synonym —Common facial paralysis

Definition —Paralysis of the facial nerve coming on acutely and not associated with any other lesion

Ætiology —The pathogenesis of Bell s palsy has been the subject of considerable discussion but the work of Ballance and Duel confirmed that the nerve was compressed just within the styloid foramen Inflammation of the fibrous tissue around the nerve outside the facial canal is believed to cause swelling of the nerve with the result that the nerve strangulates itself at the foramen The inflammation of its fibrous sheath may have spread some millimetres up the facial canal before this occurs because Ballance and Duel found scarring and contraction of the sheath extending for 4 or 5 mm when the lower portion of the canal was opened up As the chorda tympani nerve leaves the facial canal 2 to 3 mm above its termination the lesion may extend up far enough to involve it

Bell s palsy may occur at any age but is commonest between 20 and 50 The sexes are equally affected and no predisposing factors are known

Symptoms —The onset is usually rapid and sometimes even sudden Pain of a neuralgic character below the ear behind the mastoid process or referred to the occipital region is common but it does not last more than a few days and sometimes pain is entirely absent. On deep pressure upon the styloid region behind the ramus of the jaw on both sides one can almost always elicit the fact that there is tenderness on the paralysed side and sometimes obvious swelling of this region may be felt The first sign of the facial paralysis is that the patient feels the face to be stiff when he attempts to move it Subsequently the paralysis appears rapidly and the face is drawn over to the opposite side The paralysed side is motionless according to the degree and distribution of the paralysis if incomplete and if complete is expressionless The eye cannot be closed and there is epiphora from paralysis of the tensor tarsi The paralysis at the corner of the mouth causes difficulty in articulation and escape of fluids on drinking but the patient soon learns to overcome these disabilities When the paralysis is partial it is nearly always the lower part of the face which is the most affected The facial muscles soon become hyperexcitable to mechanical stimuli In nearly all the severe cases there is loss of taste over the anterior part of the tongue

There is never any pain in the distribution of the facial nerve After a time which may vary from a few days to 2 years the paralysis begins to recover and invariably this recovery appears in the upper facial region first

In not a few cases however recovery remains imperfect and a degree of contracture occurs in the paralysed muscles with the result that the corner of the mouth ceases to droop and at rest the asymmetry of the face is not marked though with movement the limited action of the affected side is apparent

In rare instances Bell s palsy occurs more than once in the same individual and not necessarily on the same side It is conceivable that the true Bell s palsy may sometimes be bilateral but when bilateral facial paralysis occurs infective polyneuritis should be suspected and other signs sought for

Diagnosis —Care in diagnosis is most important since there are many causes of facial paralysis and few of them have as favourable a prognosis as Bell s palsy Facial paralysis from caries of the temporal bone rarely makes any recovery and it is usually associated with partial deafness A general examination of the nervous system should be made in every case and if any other abnormal signs are found the facial paralysis is most probably due to some cause other than Bell s palsy Again cases of facial paralysis that are slow in their onset are not cases of Bell s palsy

Facial paralysis from herpes of the geniculate ganglion —Among the not infrequent

causes of facial palsy must be numbered geniculate herpes to which attention was first drawn by Ramsay Hunt The herpetic vesicles preceded by local pain, appear in the external auditory meatus and adjacent parts of the pinna (and sometimes also just behind the pinna) and on the soft palate and anterior pillar of the fauces When the innervation of the last named derives fibres from the geniculate ganglion the clinical picture of geniculate herpes is apt to be a misleading one if it be not thought of The patient complains of pain in the ear, and in the throat on the same side As the eruption develops the fauces on the affected side are red and injected and several small ulcers (ruptured vesicles) may be seen At the same time the vesicles appear in the ear rupture and give off a watery discharge which may be mistaken for otorrhœa The pinna may then swell very considerably After some days during which the patient may feel ill and be feverish (temperature 100° to 103° F) facial paralysis develops and usually becomes complete within 12 hours Tinnitus vertigo and a varying degree of deafness are usually present In milder cases there may be only initial pain in the pinna and the appearance of herpetic vesicles on the pinna without much swelling It is in the severe cases that an erroneous diagnosis of *middle ear disease with otorrhœa may be made and hazardous and unnecessary steps* be taken to deal with this According to Ramsay Hunt facial palsy always follows geniculate herpes and undoubtedly many cases of this kind, where the herpetic eruption is minimal escape accurate diagnosis

Course and Prognosis—Recovery of Bell's palsy can in general be promised with some reservation as to its completeness particularly in elderly subjects The date of recovery is often difficult to forecast. If at the end of a week after the onset there is the slightest trace of any voluntary power in the orbicularis palpebrarum which is the ultimum moriens of the facial muscles, or if any trace of faradic excitability to bearable stimuli remains then it may be confidently said that recovery will be complete and rapid within 3 months and that there will be no contracture Cases in which no complete paralysis occurs in any region of the face usually recover in a fortnight In complete cases with complete reaction of degeneration in the muscles it is difficult to say when recovery will occur or when the effect of contracture will be at an end Cases which show no loss of taste and therefore in which there is no great extension of the inflammatory process up the *facial canal*, usually recover rapidly

In cases with imperfect recovery either continuous spasm or intermittent twitching of the partly recovered muscles may occur and may persist indefinitely causing disfigurement and discomfort

Treatment—In the acute stage salicylates and iodides may be given internally and warmth or a counter irritant such as tincture of iodine applied behind the angle of the jaw The patient should stay in the house for the first week and gentle massage may be given to the paralysed side of the face When paralysis seems to be complete undue stretching of the paralysed muscles may be minimised by splinting' the face for this purpose a silver wire rubber covered where it turns round the lip may be bent so as to hook round the lip at one end and over the ear at the other so that the mouth is kept symmetrical during facial movements Gentle massage should also be continued

It is customary to give galvanic stimulation to the paralysed muscles but if it is employed *the onset of contracture must be watched for and* the applications stopped at the first sign of it

Ballance and Duel recommended that at an early stage the lower portion of the facial canal should be opened up and the nerve thus decompressed This operation should certainly be considered if by the end of a month no sign of recovery has shown itself either to clinical examination or to electrical testing

When complete paralysis persists after a year no recovery can be expected and the disfigurement can be relieved by one of the varieties of sling operation

2 PERIPHERAL FACIAL SPASM

Synonym —Facial Hemispasm

Definition —A unilateral malady of the facial nerve in which intermitting spasm of the facial muscles occurs exactly like that caused by faradism of the facial trunk Rarely it is associated with a slowly oncoming facial paralysis and may follow a facial paralysis due to injury

Ætiology —This malady occurs in adults and the onset is usually insidious and without known cause It is most often seen in middle aged women

Symptoms —It commences with twitching of some part of the facial musculature which occurs at first at rare intervals and subsequently becomes more and more frequent so as in some cases to be almost continuous Commencing locally usually around the eye it tends to spread so as to involve the whole face in a sudden and hideous contortion The attacks of peripheral facial spasm may at first glance resemble a Jacksonian fit of the face The spasms may be so severe and continuous as to keep the eye closed for long periods together and to interfere greatly with the work and enjoyment of life The malady is associated with no other symptoms Cases exist in all degrees of severity from the mildest in which an occasional flicker of the face occurs to the most severe and incapacitating and unsightly malady

Treatment —In severe cases the only remedy which affords relief is division and alcoholic injection of some of the branches of the facial nerve in the pes anserinus or possibly of the whole of the nerve at the stylo mastoid foramen or as it crosses the ramus of the jaw The resulting paralysis and disfigurement if a large part of the nerve is divided will call for a cosmetic operation As long as the spasm is mild, such treatment is obviously worse than the disease No other treatment has any effect on the spasm but sedatives may enable the patient to bear it with less distress

THE AUDITORY AND VESTIBULAR NERVES

The eighth nerve consists of two groups of fibres different in their functions and in their origins and terminations one group arising in the cochlea and terminating in the cochlear nuclei in the pons is called the auditory or cochlear nerve the other arising from the labyrinth and ending mostly in the vestibular nuclei is called the vestibular nerve

Lesions of the auditory nerve (as well as diseases of the cochlea) give rise to two symptoms nerve deafness and tinnitus

Nerve deafness is distinguished from deafness due to middle ear disease by the fact that hearing is diminished or lost whether the sound be conveyed by air conduction or by bone conduction whereas in middle ear deafness the hearing by bone conduction is increased Weber s test consists in the application of the base of a vibrating tuning fork to the middle of the forehead the patient being asked in which ear the sound seems the louder with middle ear deafness the sound is heard better on the affected side while with inner ear or nerve deafness the opposite is the case or the patient does not appreciate any difference between the two sides For Rinne s test the fork is applied first to the mastoid process and when the patient ceases to hear *it is held at the external auditory meatus in nerve deafness the sound may be heard* by air conduction after it has become too feeble to be heard by bone conduction while in middle ear deafness the opposite obtains As a symptom of nervous disease nerve deafness is met with in cases of tumour of the eighth nerve following epidemic meningitis in syphilis of the nervous system especially *congenital syphilis* and in disease of the lateral region of the medulla

Tinnitus is a subjective sensation of noise in the ears or in the head It seems to

be due to disease of the cochlea or auditory nerve of a slow degenerative nature and though at first intermittent it usually becomes continuous before long It may also be produced temporarily by certain drugs of which quinine and salicylates are the commonest

The sounds commence faintly and at first may be perceived only in stillness and silence at night and later become louder and more persistent, and are often absolutely continuous The noise complained of may be high pitched or low pitched a piercing whistle or a hiss or even a rumble in some cases it is more elaborated and is described as like machinery or again ' bell like

In the course of time the hearing becomes impaired and in some patients vertigo occurs and may be associated with periods of aggravation of the tinnitus Medical treatment produces little benefit but sedatives such as phenobarbitone, may enab' the patient to tolerate the noise better Division of the eighth nerve often cures the tinnitus, but the patient must be warned both that it may fail to do so and that in any case the operation will produce complete deafness on the side on which the operation is performed

The most prominent symptom which results from lesions of the vestibular nerve (as well as from disorders of the labyrinth) is *vertigo* The word by derivation means 'a turning , and with vertigo of labyrinthine and vestibular nerve origin there is always a sense of rotation either of the surroundings or of the patient himself the room may seem to rotate about a vertical or a horizontal axis and there is often a disorder of projection so that when the patient falls it seems to him that the floor has come up to strike his head

It must be noted that the vast majority of patients who complain of giddiness or dizziness do not suffer from true vertigo Nearly all those who suffer from functional nervous disturbances complain of what they call dizziness, by which they mean a momentary sensation of unsteadiness objectively such a patient is not unsteady and this sensation never causes him to fall Patients suffering from generalised cerebral arteriosclerosis complain of a similar sensation as also do those who are suffering from the after effects of head injuries

With true vertigo unless it be minimal nystagmus is always present while the vertigo is going on Usually the nystagmus is seen with deviation of the eyes towards the side of the lesion but with irritative lesions of the labyrinth *e g* for a day or two after operations on the ear and with labyrinthitis the nystagmus is towards the opposite side

Tests for vestibular lesions—1 Barany s caloric test is made by irrigating the external auditory meatus with either hot or cold water or air With an intact vestibular mechanism this causes irritation of the vestibular apparatus with the appearance of nystagmus on lateral deviation of the eyes When the vestibular mechanism is impaired this test fails relatively or completely

2 If the patient be rotated either by placing him in a special rotating chair or by turning him round several times in the standing position lateral conjugate deviation of the eyes immediately after the rotation will show nystagmus in the opposite direction to the rotation if the labyrinth on that side is intact It will not appear if the functional activity of the vestibular mechanism is deficient

RECURRENT VERTIGO

The causes of recurrent vertigo are various It is necessary in every instance to make sure that there are no indications of disease of the cerebellum brain stem or cerebello pontine angle but in the great majority of cases the symptom arises from disease of the labyrinth or vestibular nerve and the following conditions have been identified (1) Meniere s disease (2) vestibular neuronitis (Dix and Hallpike) (3) positional vertigo

1 MÉNIÈRE S DISEASE

Definition —A malady in which paroxysmal attacks of labyrinthine vertigo occur at irregular intervals associated with tinnitus and progressive deafness and due to disease of the labyrinth of a chronic nature

Ætiology —Ménière s original hypothesis was that hæmorrhage into the labyrinth was the responsible factor but this is inherently improbable and lacks pathological support According to Hallpike the essential lesion is a gross distension of the endo lymph system together with degenerative changes in Corti s organ and the presence of albuminoid coagula throughout the endolymph spaces He regards these changes as incompatible with an infective origin and as probably primarily degenerative in nature

The precipitating causes of the attacks are unknown and in the absence of precise knowledge disturbances of fluid balance allergy and migraine have all been incrimin ated in some instances the attacks are associated with diarrhœa

Symptoms —The majority of cases are much milder than those described by Menière and the symptoms may be subject to long remissions

In the severe cases of the classical type the attacks set in suddenly with a buzzing noise in the ears followed immediately by intense vertigo both subjective and objec tive The vertigo may be so severe that the patient feels he is hurled to the ground He often falls as if shot but sometimes he has time to assume the sitting or lying position before the vertigo reaches its height Consciousness may rarely be impaired for a few moments Spontaneous nystagmus occurs to the side of the lesion and unilateral cerebellar signs on the side of the lesion The patient becomes nauseated and often vomits repeatedly The skin is pale and covered with a clammy sweat The patient lies perfectly still and in terror lest the least movement should bring on more vertigo The duration of the attack is usually between 15 minutes and an hour but the patient may take several hours to recover completely Sometimes the attacks are excited by sudden movement such as coughing or sneezing but they are usually without any such antecedent They may occur during sleep and wake the patient In the milder cases the vertigo is not infrequently present when the patient wakens in the morning and becomes apparent to him as soon as he moves It is not spon taneous but is brought on by movements of the head and it is also influenced by the posture of the head being worse when the affected ear is on the pillow The vertigo passes off within half an hour or an hour or two

Menière s disease is characterised by a slow onset of nerve deafness and by the time the first attack of vertigo occurs an impairment of hearing and some tinnitus are usually present If the disease is persistent there is a gradual deterioration both of vestibular and of auditory function in the affected ear and in some cases the laby rinth becomes defunct and the attacks cease

Diagnosis — This presents no peculiar difficulty for the symptoms are highly characteristic and although variable in degree are usually quite definite in the first attack The rapid disappearance of the vertigo is striking Vertiginous attacks from all other causes must be excluded In acute cerebellar lesions (including thrombosis of the posterior inferior cerebellar artery) the symptoms are very like those of laby rinthine vertigo but they are not transitory in a few hours A careful search of the nervous system for signs of organic nervous disease should in every case prevent any mistake Vertiginous attacks due to epilepsy rarely cause difficulty in the differential diagnosis because the loss of consciousness and probably the convulsive and other features of the epileptic attack are apparent

Prognosis —Most cases recover perfectly with slight impairment of hearing or have long periods of remission Some cases however go from bad to worse in spite of treatment and progressive deafness ensues with eventual disappearance of the attacks

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Symptoms—When fully developed the malady consists in paroxysms of shooting pain of great severity in the region of the throat and ear The exciting stimulus is commonly the act of swallowing But just as in trigeminal neuralgia the pain may at first be confined to a single branch of this nerve so in glossopharyngeal neuralgia the pain may for long be confined to the tympanic branch the pain being felt deep in the ear This pain does not spread to the pinna In other cases pain in the faucial region predominates the pharyngeal branches being affected As in trigeminal neuralgia the patient may enjoy long intervals of freedom from pain During a paroxysm the patient screws up his face and may hold his head in his hand as does the subject of trigeminal neuralgia

Diagnosis—The presence of neuralgic pain of great severity provoked by the act of swallowing and in its general characters and behaviour resembling the very familiar and characteristic paroxysms of trigeminal neuralgia but different from these in its restriction to the ear and throat occurring also in the absence of objective signs of a lesion of the cranial nerves these together are the features which make a diagnosis of glossopharyngeal neuralgia possible and easy

Treatment—In the early attacks the same forms of medication as are used in trigeminal neuralgia may be employed If the pain does not respond to these then surgical measures are called for and the operation usually performed is avulsion of the nerve high in the neck

THE TENTH OR VAGUS NERVE

This is a mixed nerve The motor fibres supply the voluntary muscles of the soft palate (except the tensor palati) pharynx and larynx in conjunction with the accessory fibres and also the non striped muscles of the respiratory and alimentary tracts

The sensory fibres of the vagus supply the respiratory tract the pharynx and œsophagus Its visceral fibres supply the lungs heart and abdominal viscera No sensibility seems to be supplied to the abdominal viscera by this nerve since with division of the spinal cord above the offshoot of the splanchnic nerves all sensibility in the abdomen is lost

LESIONS OF THE VAGUS

The important signs of lesion of this nerve and its nuclei are pharyngeal and laryngeal paralysis and loss of sensibility Symptoms indicative of lesions of its complicated and mysterious visceral supply are neither well marked nor well understood and in unilateral lesions seem to be entirely absent they are therefore not considered

Lesions of the vagus in the medulla are common Syringomyelia when affecting that region usually involves the nucleus ambiguus causing unilateral palsy of palate pharynx and larynx Thrombosis of the posterior inferior cerebellar artery which supplies that region of the medulla containing the nucleus ambiguus is likely to produce vagus paralysis of the same side Progressive muscular atrophy in the form of progressive bulbar paralysis may affect its cells Lesions of the nerve roots often occur from tumours of the lateral region of the medulla, and growths outside the medulla arising from nerve roots or meninges and here the lesion of the vagus roots is associated usually with those of the glossopharyngeal spinal accessory and hypoglossal In the neck penetrating wounds and growths may implicate the nerve and in the thorax tumours particularly aneurysms and new growths are apt to cause paralysis of the muscles supplied by its recurrent branch

Unilateral pharyngeal paralysis—This is characteristic of all unilateral lesions of

Treatment—Sedatives have a pronounced palliative effect The most commonly used drug is phenobarbitone, and doses of gr ½ taken three or four times daily usually bring about prompt amelioration Bromides in doses of gr 10 to 15 three times a day are equally serviceable and Gowers advocated the use of sodium salicylate or aspirin Other measures include a salt free diet, careful regulation of the bowel to prevent diarrhœa and the use of anti histamine drugs Dimenhydrinate (Dramamine) is believed by some to have a selective action as a sedative on the labyrinth

When medical treatment fails surgical measures may give relief the principal operations employed being division of the vestibular nerve partial removal of the membranous labyrinth and total destruction of the labyrinth of one side

2 VESTIBULAR NEURONITIS

In this condition the cause of the vertigo is believed not to be in the labyrinth but in the neurones of the vestibular nerve There is no disturbance of hearing In a large proportion of cases there is an associated infection in the nasal sinuses or elsewhere or the onset is associated with some febrile illness The disorder affects chiefly patients in the age group 30 to 50 without preference for sex

The attacks of vertigo are similar to those of Menière s disease but are in general less severe

Treatment consists in the administration of phenobarbitone as for Menière's disease and the removal of any local or general infection which can be discovered With these measures the liability to vertigo usually passes off in the course of a few months

3 POSITIONAL VERTIGO (POSITIONAL NYSTAGMUS)

In this variety the vertigo always occurs when the head is put in a particular position, and in most instances the exciting position is with the head back and somewhat tilted to one side Many of the cases are subsequent to head injury

The condition can usually be identified by the patient s complaint that he becomes dizzy when he turns his head (face) upwards, but specialised tests are necessary to confirm the diagnosis

Treatment consists as before in the use of phenobarbitone and in most cases the symptoms pass off completely in 3 to 12 months

THE NINTH OR GLOSSOPHARYNGEAL NERVE

Lesions of this nerve involve loss of taste over the posterior one third of the tongue with some unilateral paresis of the pharynx It is rarely involved alone in association with the other nerves taking origin in the neighbourhood it may be affected by tumours of the lateral region of the medulla and by syringomyelia

GLOSSOPHARYNGEAL NEURALGIA

Definition—A comparatively rare form of neuralgia within the distribution of the glossopharyngeal nerve It is strictly comparable with trigeminal neuralgia in the quality and severity of the pain its paroxysmal incidence the remissions in its course its provocation by special stimuli and finally by the absence of any discoverable lesion in or loss of function of the nerve

Ætiology—Nothing is known of its ætiology It is most frequently seen in middle aged or elderly males A symptomatic neuralgia of the same distribution is occasionally found in cases of carcinoma of the tongue in which the growth invades the faucial region

of the weakness the shoulder falls a little the scapula moves slightly laterally and by the unopposed action of the rhomboids and levator anguli scapulæ it is rotated the lower angle moving medially

THE TWELFTH OR HYPOGLOSSAL NERVE

The hypoglossal nerve supplies all the muscles of the tongue both intrinsic and extrinsic.

A lesion of one hypoglossal nucleus in the medulla gives rise to fibrillation and eventual atrophic paralysis of one half of the tongue When the hypoglossal nerve is divided the fibrillation is usually not apparent but the atrophy occurs more quickly and there is a loss of faradic excitability In either event the tongue becomes sickle shaped with the concavity on the paralysed side There is little impairment of movement within the mouth and no defect of articulation but the tongue turns to the paralysed side when protruded Such hemiatrophy of the tongue occurs in syringo bulbia and in syphilitic conditions tumours of the lateral region of the medulla and just lateral to it are rarer causes of it The hypoglossal nerve may be severed as a result of wounds or operations in the neck

Atrophic paralysis of the whole tongue occurs when both hypoglossal nuclei are affected and is commonly seen in progressive bulbar paralysis Protrusion of the tongue is impossible and articulation is greatly impaired but this may be partly due to other paralyses which are usually associated

Upper motor neurone paralysis of the tongue is not uncommon A patient suffering from motor aphasia is commonly unable to protrude his tongue and in bilateral hemiplegia and the condition known as pseudo-bulbar paralysis, the tongue is in a state of spastic paralysis neighbouring parts are similarly affected and well-marked dysarthria and dysphagia are frequent The tongue appears contracted but there is no real wasting and no loss of electrical excitability

THE SIGNS OF LOCAL LESIONS WITHIN THE SKULL AND BRAIN

In this chapter we must be content with a brief consideration of the signs and symptoms upon which we depend for the localisation of cerebral lesions We may take first the various regions of the brain and secondly as we have to deal not only with lesions within the brain but also with lesions within the skull that may be out side the brain itself we will consider the symptomatology peculiar to lesions in the three cranial fossæ

THE CEREBRAL HEMISPHERES

GENERAL LATERALISING SIGNS

A lesion within or involving one cerebral hemisphere may reveal by the signs it produces whether it is right or left sided without affording further evidence of its localisation Such signs are unilateral loss or diminution of the abdominal reflexes unilateral accentuation of the tendon reflexes an extensor response or just perceptible unilateral paresis of movement of the lower part of the face Fits starting unilaterally, or with turning of the head and eyes to one side may be of similar significance

the vagus high up It is recognised by the low lying motionless palate and the loss of sensibility of one side of the pharynx with loss of the pharyngeal reflex on that side There is no impairment whatever of deglutition When the soft palate is elevated as in saying Ah! it is pulled over to the sound side.

Bilateral pharyngeal paralysis—This results from nuclear lesions of the nucleus ambiguus on both sides and is also common in diphtheria polyneuritis myasthenia gravis and progressive muscular atrophy The whole palate is low and paretic or paralysed the voice is nasal there is nasal regurgitation of liquids, the cheeks cannot be forcibly blown out and there is difficulty in pronouncing final 'k and g, the words 'kick and egg' becoming *kich* and '*enck*

Total unilateral laryngeal paralysis—Since the superior laryngeal nerve which supplies the crico thyroid muscle (the chief tensor and adductor of the vocal cords) is given off high in the neck from the ganglion of the trunk of the vagus it follows that total paralysis of the larynx on one side can only result from a lesion of the vagus between the ganglion of the trunk and the nucleus ambiguus in the medulla The vocal cord on the paralysed side becomes motionless in the cadaveric position—that is, midway between the abduction and adduction The larynx is insensitive on the same side There is some loss of tone of voice but no stridor.

Unilateral abductor paralysis or recurrent laryngeal paralysis—This occurs from all lesions of the trunk of the vagus below the ganglion of the trunk and from lesions of the recurrent laryngeal branch The vocal cord on the side of paralysis lies close to the mid line it fails to abduct when the patient takes a deep breath there is no change of voice but there may be slight stridor on inspiration The sensibility of the larynx is not affected

Bilateral abductor paralysis—This condition is occasionally seen as a complication of thyroidectomy and in malignant disease of the thyroid gland It occurs also in bilateral lesions of the recurrent laryngeal nerves in the thorax which may occur from aneurysm and new growths It is the most dangerous form of laryngeal palsy as the vocal cords cannot be abducted and they tend to suck together during inspiration for this reason bilateral abductor paralysis may cause death from asphyxia *or necessitate tracheotomy*

THE ELEVENTH OR SPINAL ACCESSORY NERVE

This nerve may be caught with the vagus by lateral lesions outside the medulla or by lesions in the region of the jugular foramen but it is more often damaged by injuries to the neck and by operations for the removal of cervical glands The spinal accessory nerve as it crosses the posterior triangle of the neck is very liable to injury either from blows or from sudden strains and most of the isolated trapezius palsies are due to local neuritis of the nerve trunk so arising

When the sternomastoid is paralysed there is neither complaint by *the patient* of weakness *nor deformity nor peculiar attitude of the neck* other muscles compensating for its paralysis The muscle does not harden when the head is turned to the side opposite to the paralysis and its reaction to faradism is diminished or lost

Paralysis of the trapezius on the other hand causes great disability in raising the arm above the horizontal level of the shoulder and also difficulty in shrugging the shoulder or approximating the scapula to the middle line behind and therefore also in carrying the extended arm backwards But the only part of the trapezius that is completely paralysed by disease of the spinal accessory nerve is the highest portion Instead of its normal nearly straight contour the neck presents on the affected side a concave curve and the difference between the two sides is brought out more strongly by a deep inspiration The other parts of the trapezius are weakened but not paralysed since they receive additional innervation from the cervical nerves In consequence

In such cases the patient becomes completely apathetic silent and immobile lying with open eyes, but displaying no initiative of any kind

SYNDROMES OF THE CENTRAL REGION (REGION OF THE MOTOR CORTEX ')

Hemiplegia is the characteristic symptom of a paralytic lesion in this portion of the hemisphere and the Jacksonian fit that of an irritative lesion

The Jacksonian, or focal fit most commonly originates in the face, thumb or big toe and thence spreads with varying rapidity until much or all of the corresponding side of the body is affected It may then become generalised Consciousness is commonly preserved in attacks which remain unilateral Such a fit may be accompanied by conjugate deviation of the head and eyes away from the side of the lesion and may be followed by a transient hemiparesis or in the case of a tumour by a progressive and permanent hemiplegia The hemiparesis resulting from a destructive lesion near the surface will affect face arm or leg predominantly according to the site of the lesion The more deeply this extends into the underlying white matter the more will the weakness affect the whole half body since the pyramidal fibres converge from the cortex towards the capsule Disturbances of cortical sensibility corresponding in distribution to the motor defect are not infrequent and result from simultaneous involvement of the neighbouring post central convolution

PARIETAL LOBES

Irritative lesions in this area may give rise to focal fits heralded by subjunctive sensory disturbances on the opposite side These are usually described as consisting of numbness tingling or pins and needles and may spread in an orderly manner to other parts of the affected side of the body in the same way as the muscular spasm in discharging lesions of the motor cortex Destructive lesions in this neighbourhood may be marked by a characteristic series of sensory disturbances These include defective localisation of tactile stimuli defective appreciation of two simultaneous contacts (Weber s compass test) defective appreciation of three dimensional space (i e size and form) There is in addition defective power of differentiating minor differences in intensity of painful or thermal stimuli and a ready fatigue of sensory functions The simple recognition of such stimuli may be relatively intact It will be seen that the defects in spatial discrimination which result from these modes of sensory loss lead to that inability to recognise and identify objects held in the hand or to describe their size shape or texture which is known as astereognosis The appreciation of movement and of position is apt to be faulty and some ataxy commonly results Disturbances of attention may also occur on the contralateral side of the body together with failure of spatial orientation and of recognition of the body image In left sided lesions there may in addition be disorders of the visual speech function resulting in dyslexia agraphia and acalculia Trophic changes particularly decrease in size of the muscles may be seen in the periphery of the limbs and this may be so marked as to amount to true muscular wasting

OCCIPITAL LOBES

Lesions of the cuneus and region of the calcarine fissure on the mesial aspect of the occipital lobe result in hemianopia of the opposite field but central vision escapes Gordon Holmes showed that if the lesion is limited above the calcarine fissure a quadrantic hemianopia of the lower field results and if the lesion is below the calcarine fissure the quadrantic defect resulting is of the upper field Since central vision is represented at each occipital pole a lesion of either pole causes contralateral,

THE FRONTAL LOBES

These consist of the portions of the hemispheres anterior to the coronal sulci (*fissures of Rolando*) and thus include the ascending frontal convolutions and the portions of the hemispheres anterior to them (*the 'prefrontal' areas*) The lesions to be met with in the prefrontal areas include tumour abscess and thrombosis of the anterior cerebral artery the last named being comparatively rare

The syndrome of the anterior cerebral artery consists of a spastic weakness of the opposite lower limb, especially in its distal part with the appropriate changes in its reflexes Sometimes there is slight weakness of the corresponding arm which may be associated with forced groping and grasping in the arm on one or both sides The face is seldom affected Apraxia of the left arm has been described and there may be some drowsiness and mental confusion

The syndrome of frontal lobe tumour.—The area of the frontal lobes anterior to the ascending frontal convolutions (the prefrontal areas) comprises a considerable portion of the cerebrum and is frequently the site of tumour formation The symptoms produced vary greatly with the rapidity of growth of the tumour and with other factors imperfectly understood As a rule an early if not the initial symptom, is a change in the patient s mental state He becomes apathetic and lacking in initiative The association and flow of ideas tend to fail He sits about idly, lacks attention and becomes indifferent to cleanliness and other aspects of personal behaviour He is apt to permit the unhindered passage of urine and even of fæces and to be totally insensitive to the embarrassments such conduct normally involves This form of incontinence is in fact a diagnostic symptom of great value in frontal lobe tumours Rarely, the patient develops an abnormal facetiousness and euphoria—the so called 'Witzelsucht' These early symptoms may gradually give place to a profound dementia

Movement is often disordered by the development of apraxia and sometimes by that of forced groping and grasping which when unilateral is a useful sign of frontal lobe involvement When bilateral it is of less localising significance and may be met with in diffuse degenerative or neoplastic lesions of the hemispheres and in cases of severe internal hydrocephalus Such grasping and groping has been shown to consist of two components (i) Volitional grasping movements made by the conscious patient when some object is felt by him in his palm or is seen by him to approach his hand These movements wane and cease when consciousness is failing or when attention is defective (ii) A true tonic reflex grasp of any object held in the hand if this object be pulled away in such a manner as to put the flexors of the fingers on the stretch The flexors tighten as the pull is maintained and their contraction may attain great force such indeed that sometimes the patient can be pulled out of bed by this involuntary grasp which he is unable voluntarily to relax This reflex may persist even after consciousness is lost but is abolished by injection of novocaine into the appropriate afferent nerves Fits are a common feature of frontal tumours and may be generalised from their onset or start with turning of the head and eyes to the opposite side Attacks of petit mal are not uncommon If the orbital lobule be involved there may be unilateral anosmia or direct pressure on the optic nerve causing unilateral failure of vision associated with primary optic atrophy This when combined with papillœdema in the opposite eye has been described as Foster Kennedy s syndrome These symptoms will be further considered in connection with the syndrome of the anterior cranial fossa

As the tumour expands it is likely to encroach upon the projection pathway from the motor cortex with a resulting contralateral hemiparesis and when left sided it is commonly associated with a predominantly executive disturbance of speech Tumours in the medial portions of the frontal lobes may come to involve the corpus callosum and frequently spread through this structure to the opposite hemisphere

In such cases the patient becomes completely apathetic silent and immobile, lying with open eyes but displaying no initiative of any kind

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central homonymous hemianopic scotomata vision in the periphery of the field remaining intact Similarly a bilateral lesion involving both occipital poles will result in bilateral central scotomata *and a bilateral lesion of the calcarine region will produce* blindness of both peripheral fields, central vision remaining intact If the lesion extends deeply into the occipital lobe so as completely to sever the optic radiation to the occipital cortex complete hemianopia affecting both the peripheral and central parts of the visual fields will result The hemianopias resulting from a lesion of the occipital lobes have been distinguished from those due to lesions of the optic tracts by the fact that in the former the pupils react to light thrown on to the blind part of the field (Wernicke s hemianopic pupil phenomenon) To be of practical value this test needs to be made with a very narrow pencil of parallel rays to avoid the effects of dispersal of light within the eye

On the outer surface of the occipital lobe a lesion on the left side may sever the connections between the visual centres and the speech centres and so produce word blindness Bilateral lesions in this region may be associated with visual disorientation

Jacksonian attacks are often of great value in the localisation of occipital lobe lesions When the lesion is situated posteriorly these take the form of undifferentiated visual *hallucinations* such as flashes of light or coloured figures *When the lesion* is situated more anteriorly at the junction of the occipital and temporal lobes the visual hallucinations may take the more elaborate form of visions of people animals or places In either case the hallucinations may be accompanied or followed by a transient hemianopia

TEMPORAL LOBES

The considerable portion of the cortex comprised by the temporal lobes includes the cortical representation of the functions of smell taste and hearing and on the left side in normal right handed persons the function of speech

The uncinate and hippocampal regions of these lobes are the cortical seats for taste and smell and the localising symptoms which are rarely absent when lesions in these regions exist are Jacksonian attacks taking the form of hallucinations of taste and smell nearly always of an unpleasant character The hallucination is often accompanied or immediately followed by a dreamy state in which the patient *may* experience a feeling of strangeness or of intense familiarity or a panoramic recall of events of his past life This tate of altered consciousness may be accompanied by smacking of the lips or champing of the jaw The senses of taste and smell are not lost from a unilateral lesion of this region since they are bilaterally represented in the cerebral hemispheres Recent clinical and electro encephalographic researches indicate that discharging lesions in the temporal lobes play an important part in epileptic automatism and the so called psychomotor epilepsy It also seems likely that congenital or acquired defects in the temporal lobes may be concerned with the behaviour disorders of aggressive psychopaths

The outer surfaces of the temporal lobes are concerned with hearing Lesions here may re ult in fits which are heralded by crude auditory hallucinations but owing to the complete semi decussation of the auditory path unilateral lesions never produce detectable deafness Bilateral lesions may however produce cortical deafness

In right handed subjects lesions of the left temporal lobe commonly give rise to serious disorders of speech *function With lesions situated far forward* towards the insula the disturbance is predominantly one of spoken speech With those situated in the posterior portion of the lobe the defect is predominantly one of the reception of speech Deeply situated lesions of the temporal lobe commonly produce jargon aphasia Transitory disturbances of speech may occur in focal attacks originating from lesions in this area

On account of the wide excursion which the optic radiation makes into the deep

part of the temporal lobe in its course from the thalamus to the calcarine cortex homonymous field defects especially of the upper quadrants are very common in deep seated lesions of the temporal lobes Such lesions may also produce a paresis for emotional movements of the opposite half of the face which is relatively greater than the loss for voluntary movements The occurrence of incontinence of sphincters of a mental type is occasionally seen

INTERNAL CAPSULE

In this region the chief motor tract is condensed into a small space and is situated immediately in front of a narrowly localised sensory tract while not much farther posteriorly the visual path emerges from the thalamus Lesions of this region therefore produce severe and widely spread hemiplegia of the opposite side often associated with hemianæsthesia and not infrequently with hemianopia of the opposite side From the proximity of the thalamus and corpus striatum there is often involvement of these structures in a capsular lesion with appearance of the characteristic spontaneous involuntary movements and sensory loss

THE REGION OF THE FALX CEREBRI

Lesions of this region are likely to affect both hemispheres equally Tumours opposite the paracentral lobules may cause bilateral crural monoplegia with disturbances of cortical sensibility in the feet if the post central area is involved Focal fits starting in one foot may occur Disturbances of sphincter control are occasionally seen Tumours arising from the posterior region of the falx may result in bilateral hemianopia Thrombosis of the superior longitudinal sinus may produce widespread bilateral lesions of the hemispheres with double hemiplegia in which the face and hands are usually spared

BASAL GANGLIA

OPTIC THALAMUS

A very characteristic clinical picture results from destruction by thrombosis of this structure which is termed the thalamic syndrome of Dejerine and Roussy there is hemiparesis with spontaneous involuntary movements on the side of the body opposite to the damaged hemisphere The latter may be of the nature of tremor, intention tremor choreic athetotic dancing or irregular movements Mo t post hemiplegic involuntary movements are due to a lesion of the thalamus In addition there is hemianæsthesia often with a characteristic hypersensitivity to painful thermal or other stimuli such as tickling rubbing etc which may produce agonising distress Sometimes spontaneous constant and unrelievable pain occurs on the affected side of the body Emotional movement of the face may be impaired much more than is volitional movement The thalamic syndrome is not invariably or even commonly seen when the lesion is a tumour In such cases the symptom complex varies according to whether the growth primarily ari es in the thalamus or invades it from its lateral aspect In the former case it arises in the subependymal glia and spreads laterally Such tumours are characterised by early mental deterioration with conjugate ocular palsies Sensory changes are absent or only terminal in appearance In the case of tumours secondarily invading the thalamus from its lateral side sensory changes of the order described under the thalamic syndrome of Dejerine and Roussy and by Head and Holmes are seen

CORPUS STRIATUM

Little is known with certainty of the symptomatology of focal lesions of the large masses of grey matter which form this structure The syndrome of Parkinsonism is associated with degenerative changes in the globus pallidus of both lenticular nuclei but such changes are not confined to those organs but involve other areas of the cerebral hemisphere as well The same is true of chorea and athetosis in which degenerative changes are conspicuous in the caudate nuclei However a local lesion usually vascular in a neighbouring mass of grey matter the corpus subthalamicum or corpus Luysii is followed by very violent unilateral choreiform movements on the opposite side of the body, the so called *apoplectic chorea* or hemiballismus

THIRD VENTRICLE AND HYPOTHALAMUS

Lesions occupying this cavity which are usually neoplastic may produce symptoms of localising value in addition to those resulting from obstruction of the cerebro spinal fluid circulation (hydrocephalus) The most important of these are hypersomnia diabetes insipidus obesity and alteration in primary and secondary sexual functions of a more variable character than those which occur in lesions of the pituitary body In the case of the not uncommon colloid cysts of the third ventricle which hang suspended from its roof by a short pedicle the symptoms including the obstructive hydrocephalus may be noticeably intermittent Where the posterior end of the ventricle is affected there may be disturbance of the pupillary light reflex

BRAIN STEM

THE MID BRAIN

This portion of the brain stem consists of a small dorsal area the quadrigeminal plate or tectum and a large ventral area the cerebral peduncles or crura cerebri

At the level of the corpora quadrigemina the oculo motor nuclei lie on either side of the aqueduct of Sylvius and lower down on either side of the middle line in the floor of the upper part of the fourth ventricle Lesions of this region cause nuclear ophthalmoplegia—that is paralysis of both eyes in terms of the conjugate movements upwards downwards or laterally From above downwards lesions of this column of oculo motor nuclei will produce reflex iridoplegia loss of convergence paralysis of upward, downward and lateral movements respectively

Immediately ventral to the third nerve nucleus and decussating below it lie the superior cerebellar peduncles passing to the red nuclei Involvement of these structures causes ataxy of the limbs and trunk

A lesion of the tectal region of the mid brain produces a characteristic syndrome of nuclear ophthalmoplegia with bilateral ataxy which is termed *Nothnagel s syndrome*

In the ventral portion of this region of the brain stem are the crura cerebri with the third nerve perforating each crus to emerge on its inner side and the optic tract running round the crus as it passes back from the optic chiasma to the lateral geniculate body A lesion of one crus will cause hemiplegia of the opposite side and paralysis of the third nerve on the same side This pathognomonic localising combination is known as *Weber s syndrome*

Situated a little more dorsally a lesion of the crus will produce ophthalmoplegia of one eye with tremor and inco ordination of the opposite limbs This is known as *Benedikt s syndrome*

Extension of a lesion outwards from the crus may cause tract hemianopia in which

the half fields are completely involved and the light reflex lost from the blind fields Interference with the fillet may cause hemianæsthesia on the opposite side

PONS AND MEDULLA

In these regions the motor and sensory tracts the middle and inferior cerebellar peduncles the cranial nerve nuclei and the outgoing cranial nerves are closely packed together and the signs resulting from destruction of these will be various combinations of spastic paralysis ataxy and sensory loss in the body and limbs—from interference with the long conducting tracts—together with nuclear and peripheral nerve palsies and anæsthesia in the distribution of the cranial nerves

If the lesion is unilateral the body and the structures innervated by the cranial nerves will be affected on opposite sides causing the crossed paralyses or alternate paralyses characteristic of lesions of the brain stem Of these facial palsy of lower motor neurone type with contralateral hemiplegia is the most frequently encountered trigeminal palsy and anæsthesia and vagoglossopharyngeal palsy with contralateral hemiplegia being less common Lesions of the brain stem below the oculo motor nuclei cause small pupils (pontine myosis) by cutting off those nuclei from the spinal cord whence the tonic dilators of the pupils—the cervical sympathetic system—emerge Lesions in the upper part of the pons commonly lead to loss of conjugate lateral movement of the eyes If the connections of the vestibular nerve are involved intense vertigo may result together with nystagmus at rest and on movement of the eyes Glycosuria may be met with in lesions in the neighbourhood of the fourth ventricle and the respiratory centre may be involved

The common lesion involving the medulla is softening of the lateral portion from thrombosis of the posterior inferior cerebellar artery or its branches the so called cerebellar apoplexy (see p 1440) Owing to the smallness of the brain stem lesions of an inflammatory or neoplastic character commonly involve both sides of the structure and bilateral symptoms result

CEREBELLUM

When lesions of this structure develop suddenly they are apt to produce more striking disturbances of function than when they develop gradually a point which it is important to remember when the presence of an abscess or a tumour within the cerebellum is suspected These disturbances are all in the realm of voluntary movement and the several different components of cerebellar ataxy are to be regarded not so much as special disorders of different cerebellar functions but as expressions of a single disorder which owe their varying appearance to the varying nature of the clinical tests employed

Hypotonia—This is particularly marked in acute lesions but can also be detected in those of slow evolution It shows itself by marked flaccidity and extensibility of the limb muscles which permit of undue mobility of the joints and leads to a modification of the normal posture of the limbs and when marked to the pendular form of knee jerk The hypotonia is largely responsible for the symptom of *dysmetria* If the patient is asked to extend the arm and pick up some object such as a glass or to touch a fixed point the limb is shot forward with undue force and may over shoot the mark Similarly the hypotonia may give rise to the *rebound phenomenon* If the arms be horizontally extended by the patient and the observer smartly strikes them downwards by a blow on the hand the arm on the normal side is quickly brought to rest in its original position with the minimum of recoil On the side of the lesion however the hand and arm ' bounce freely and may oscillate two or three times before being brought to rest

Dysdiadochokinesis —This name has been used to describe the slowness clumsiness and irregularity with which alternating movements (*e g* pronation supination of the forearm) are carried out although the simple movement can be performed normally In carrying out this test it is common to see adventitious movements in the proximal segments of the limb from disturbance of the normal co ordinated contraction of the adjuvant muscles To correct this disturbance the patient tends to break up complex movements into their several components which are carried out successively instead of simultaneously—the so called movement by numbers

Tremor —This is not a resting tremor but an unsteadiness which develops during movement and in purposive movements tends to increase in range and severity as the climax of the movement is reached It is thus essentially an intention' tremor

Similarly if the arms are out stretched they may show a tendency to droop, which is corrected by a series of jerks which thus gives the form of a tremor

Again standing there may be irregular oscillations of the trunk and head—the so called titubation

Gait —In bilateral lesions the gait has a reeling staggering character and in unilateral lesions there is a tendency to sway and deviate towards the side of the lesion The disorder may vary in severity from a slight unsteadiness to a complete inability to walk or stand unaided There is a tendency to walk with the legs abnormally separated to lessen the tendency to overbalance and the feet are brought down irregularly with a stamp

Speech —The articulatory musculature shares the inco ordination of the other voluntary muscles with a resulting characteristic dysarthria The defect is known as scanning or staccato speech It consists of slowness of articulation and a tendency to say each syllable of a word as though it were a separate word The rhythm of speech becomes irregular some syllables being slurred over others being enunciated with almost explosive violence

Nystagmus —Nystagmus is particularly frequent in those lesions of the cerebellum which involve its connections with the brain stem and the neighbouring vestibular nuclei In unilateral lesions there is coarse nystagmus on deviating the eyes to the side of the lesion with a finer and more rapid movement on deviation away from the side of the lesion In bilateral lesions the nystagmus may be symmetrical and if the lesion is confined to the superficial areas of the cerebellar hemispheres nystagmus may be entirely absent Rarely—usually after acute lesions such as gunshot wounds or operative interference—the phenomenon of skew deviation may appear temporarily the eye on the side of the lesion being displaced downwards and inwards the opposite eye upwards and outwards A slight degree of skew deviation on lateral deviation of the eyes may be seen in deeply seated tumours of the cerebellum

The cerebellum forms part of the non sensory afferent nervous system and is concerned with the co ordination of voluntary movement It is not a sensory organ and there is no disturbance of any form of sensibility in cerebellar lesions

THE ANTERIOR FOSSA OF THE SKULL

The lesion most commonly found in this situation is a meningioma arising from the dural covering of the cribriform plate and growing upwards into the olfactory groove The earliest sign is anosmia from pressure on the olfactory bulb and tract unilateral at first and later often bilateral Unilateral loss of vision associated with primary optic atrophy may later be associated with papilloedema in the opposite eye as an expression of the general rise of intracranial tension Such a tumour gradually displaces the overlying frontal lobe and may then give rise to mental deterioration and fits but only in tumours of exceptional size is a crossed hemiparesis observed

Aneurysm of the anterior cerebral or anterior communicating arteries may give rise to similar early symptoms but owing to its limited size papillœdema and the remote pressure effects are not seen

THE MIDDLE FOSSA OF THE SKULL

A rich variety of lesions may arise in or invade this fossa and the syndromes vary according to the situation of the lesion

The lesions in the mid line include pituitary adenomata tumours of the pituitary stalk and meningioma of the sellar diaphragm (parasellar and suprasellar tumours) In the lateral parts of the fossa passing from mesial to lateral we have to consider lesions in the cavity or walls of the cavernous sinus and tumours arising from the sphenoidal ridge in its middle and outer parts Finally reference must be made to growths invading the base of the skull and either occluding its foramina and producing cranial nerve palsies or actually invading the cranial cavity Secondary deposits of carcinoma and epitheliomata of the naso pharynx are the common lesions of the last named group

REGION OF THE OPTIC CHIASMA AND THE PITUITARY BODY

The most common lesion in this region is tumour of the pituitary usually an adenoma The earliest symptoms of such a tumour are of an endocrine disturbance and vary according to the nature of the tumour If this is composed of eosinophil cells acromegaly or gigantism will result whereas if the adenoma is composed of indifferent (chromophobe) cells the endocrine disturbance will take the form of hypo pituitarism of which Frohlich s dystrophia adiposo genitalis is the common and Lorain s infantilism the rarer type Basophil adenomata although producing a char acteristic group of endocrine symptoms commonly described as Cushing s syndrome (see p 516) do not attain a size sufficient to produce symptoms as space occupying lesions

When a pituitary tumour of whatever kind extends outside the cavity of the sella turcica it causes distortion of the optic chiasma and produces one of a variety of visual disturbances The commonest of these is a bitemporal hemianopia sometimes starting as bitemporal paracentral scotomata which gradually increase in size till the entire temporal fields are lost This results from the stretching of the decussating fibres of the chiasma derived from the nasal halves of each retina In other cases if the extension of the tumour is forward uniocular scotoma hemianopia or blindness may result while if the extension is backward homonymous hemianopia may result from involvement of the optic tract It cannot be too strongly emphasised that the form of the visual field defect in pituitary tumours is determined by the position of the local pressure upon the visual pathway and that while a bitemporal hemianopia is the most usual and characteristic defect the others which have been mentioned are frequently seen Primary optic atrophy in the affected eyes is the rule in pituitary tumours and papillœdema is not seen unless as rarely happens the tumour has attained such a size as to obstruct the third ventricle

Meningeal tumours arising from the sellar diaphragm and aneurysms extending backwards from the anterior communicating artery and cystic arachnoiditis may pro duce identical pressure symptoms but without the endocrine disorders of pituitary tumours

Cysts derived from vestiges of Rathke s pouch give rise to endocrine and local pressure symptoms comparable to those of primary intra sellar tumours but in addition give rise to papillœdema and internal hydrocephalus from obstruction of the third ventricle (see also p 1403)

SYNDROMES OF THE CAVERNOUS SINUS

The commonest acute lesion of this cavity is thrombosis usually septic Of the slowly developing lesions saccular aneurysm of the carotid artery is the most frequent though the cavity may be encroached upon by tumours originating from the mesial end of the sphenoidal ridge Symptoms consist of paresis of the third fourth and sixth cranial nerves often leading to complete ophthalmoplegia anæsthesia in the distribution of the ophthalmic division of the trigeminus and proptosis of the corresponding eye with œdema of the orbital tissues and conjunctiva from congestion of the ophthalmic veins In rapidly developing lesions unilateral papillœdema may occur but in those of slow development unilateral optic atrophy from pressure on the neighbouring optic nerve is more often seen

SYNDROMES OF THE SPHENOIDAL RIDGE

The dural sinus which runs along the sphenoidal ridge (sinus sphenoparietalis) is one of the sites of election of the development of meningiomata From the point of view of localising diagnosis this ridge may be divided into three parts the inner (or clinoidal) the middle and outer

A meningioma arising from the inner part gives rise in its early stages to a syndrome similar to that of a lesion of the cavernous sinus Later symptoms referable to pressure on the temporo sphenoidal lobe may occur (uncinate fits personality changes and crossed hemiparesis) Papillœdema may result from general increase of intracranial pressure

A meningioma of the middle part of the ridge may remain for long without clear localising signs and radiography and ventriculography may be necessary to establish its position

At the outer end of the ridge a meningioma may produce as its localising syndrome unilateral exophthalmos without squint some fullness of the temporal fossa with local tenderness on pressure speech disturbances if the lesion is left sided together with the general symptoms and signs of raised intracranial tension The X ray picture usually reveals densification of bone or even hyperostosis of a part of the ridge and adjoining bone

SYNDROMES OF THE BASE OF THE SKULL

The characteristic signs of such lesions are palsies of the cranial nerves often in groups anatomically close to one another without any evidence of intracerebral damage or rise in intracranial tension The common cause is malignant growth either secondary deposits from remote carcinomata the lung and breast being the most important, or direct invasion from the naso pharynx

THE POSTERIOR FOSSA OF THE SKULL

Lateral recess —The angle formed by the posterior surface of the petrous temporal bone and the tentorium (cerebello pontine angle) is a common situation for neuro fibromata which grow usually from the eighth nerve but occasionally from the fifth or seventh Rarely a meningioma may occupy the same position Such a tumour presses into the lateral lobe of the cerebellum and the side of the pons A highly characteristic clinical picture results consisting of slowly progressive nerve deafness and tinnitus some facial weakness usually accompanied by peripheral facial spasm impairment of sensibility in the area of the fifth nerve with diminution or loss of the corresponding corneal reflex and signs of ipsilateral cerebellar involvement Such

tumours are of slow growth and headaches and papillœdema are often absent or occur late in the clinical picture

APHASIA AND OTHER DEFECTS OF SPEECH

Speech is the most highly developed and recently evolved function of the human being which is capable of direct analysis Of all man s endowments it is the one which marks him off most clearly from his closest neighbours in the animal world While in its final expression speech consists of sensori motor activities of many mechanisms each simple in comparison with the whole its roots strike deeply into the texture of the mind and it constitutes the symbolic currency of thought itself indeed it is doubtful if without speech in this wider sense any but the simplest thoughts are possible So it is that we find that profound disturbances of speech function are invariably accompanied by disorder of the mind

Speech in its simplest form is a means of communication of thought between individuals by the production and perception of sounds but unlike sight or hearing it is an elastic function capable of indefinite extension and elaboration both in the race and in the individual We thus find an almost infinite variation between the simple language of a primitive people and the highly elaborate language of a civilised race between the speech of an uneducated peasant for whose simple needs a few hundred words suffice and that of a master of prose who may use thousands of words to express shades of meaning far beyond the scope of an uncultured person between the speech of a child and that of the same individual grown to maturity The growth of speech proceeds *pari passu* with the growth of the mind which employs it for its needs Furthermore upon the foundation of the initial symbolic expression of thought in spoken language has been erected in all but primitive races the further edifice of written speech in which visual symbols replace those of sound The evolution of speech in the different races of mankind is the province of the science of philology but its growth in the individual in health and its dissolution in disease make up one of the most fascinating and complex chapters of medicine As would be expected in a function of such complexity the disorders of speech are many and varied At one end of the scale are disturbances purely psychological in their origin such as hysterical mutism at the other are those due to the defects of the executive structures such as the tongue and larynx and the neuro muscular mechanisms which control them To disturbances of this order the term *dysarthria* is applied Between these extremes lie a group of speech disorders which depend upon physical disturbance of the portions of the cerebrum which form the anatomical substratum of the speech function and to these the terms *aphasia* or *dysphasia* are applied It is with this order of speech disturbance that we are at first concerned

APHASIA

General Considerations —Few subjects have suffered more from attempts at over simplification than the study of aphasia Many attempts have been made by the creation of hypothetical centres connected with one another by supposedly well defined tracts to explain the manifold and often apparently conflicting facts which may be observed in an aphasic patient Such diagrammatic analyses have been based upon individual cases of aphasia in which particular aspects of speech function have been predominately affected and in which post mortem examination has revealed damage to a circumscribed area of the brain Thus Broca s centre in the cortex of the posterior part of the left third prefrontal convolution was the motor centre for spoken speech while Exner s centre in a similar position in the second left

prefrontal convolution was the motor centre for written language The auditory word centre in which auditory memories of words were stored was in the cortex of the first and second temporal gyri while the ' visual word centre ' in which visual memories for words were impressed was in the cortex of the angular gyrus These various centres were connected together by to and fro pathways which could be separately affected by a lesion But the attempts to explain the multitudinous and varied phenomena which occur in lesions of the speech centre by assuming damage to one or other of these hypothetical ' word centres ' or to their connecting paths proved highly unsatisfactory, and the validity of such clinico pathological correlations was usually undermined by the fact that the majority of cases of aphasia result from vascular lesions in which multiple areas of disease are present or from tumours of wide extent

Clinical observation shows that as the function of speech in health evolves *as a whole* from more simple to more complex by a process of gradual elaboration so in disease it undergoes dissolution as a whole from more complex to more simple The more critically cases of so called pure motor aphasia or pure word deafness are examined the more clear it becomes that while one particular aspect of spoken speech is particularly affected, the level of speech function as a whole is lowered Furthermore, in a given case of aphasia the defect of function is not constant but may vary widely with the activity of the brain as a whole in response to such factors as fatigue attention anxiety and the general level of health of the whole individual

These considerations must constantly be borne in mind in the examination of aphasic patients and in our attempts to generalise from such individual observations and to obtain a clear understanding of aphasia as a whole

Anatomical Considerations —The function of speech seems to be concerned with the left hemisphere of the brain alone in right handed persons and this is explained by the major potential of the left hemisphere for receptivity and education associated with the major use of the right hand through the countless ages of humanity True left handedness is usually associated with a transfer of the speech function to the right hemisphere, but there are exceptions to this rule The possibilities of transfer of the speech function from the left to the right hemisphere is great during childhood to the extent that no lesion of the speech region of the left hemisphere however extensive causes lasting loss of speech in a child under the age of 6 years provided that sufficient intelligence remains to permit of re learning After this age the possibility of such compensation by the right hemisphere from lesions in the left hemisphere seems gradually to diminish and to occur but little after adult life is reached but even in adult life remarkable exceptions to this rule are seen Within the left hemisphere speech function has as its anatomical substratum a region of the cerebral convolutions having its centre a little behind the middle of the first and second temporal convolutions It is limited above by the posterior limits of the Sylvian fissure occupies probably most of the external convexity of the left temporal lobe and spreads backwards into the supramarginal and angular gyri while anteriorly it extends forward deep to the Sylvian fissure over all the convolutions of the insula and to the posterior ends of the second and third left frontal gyri

This speech region of the brain comprises not only the cortex but also the subcortical white matter which carries the paths of communication between the speech region and other portions of the brain Posteriorly it receives an important tract from the visual region of the cortex An interruption of this tract results in the condition known as pure word blindness ' in which the most conspicuous feature is an inability to appreciate written speech Upon its deep aspect the speech region of the convolutions receives the temporal projection of fibres conveying auditory impressions and destruction of this system by a *lesion undercutting the convolutions* in the centre of the temporal lobe results in serious speech disturbance in which

word deafness ' or inability to appreciate spoken language, is the most important component In this same region another set of fibres impinges upon the speech area which convey the muscular sense impressions and other sensory impressions which are produced in the movements of articulation and which are the only guidance which the deaf mute has in the knowledge of correct execution of his articulation A lesion deep in the temporal lobe may interrupt both the foregoing paths and so isolate the speech region from any appreciation of correct execution with the result that spoken language becomes unshapen and degenerates into a voluble jargon or jargon aphasia which is invariably associated with serious mental deterioration and confusion

In the anterior half of the speech area a tract of white fibres gathers by degrees, and passing forward constitutes the bulk of the temporal isthmus which joins the temporal lappet of the insula to the region beneath the middle and inferior frontal convolutions from whence it is connected with the pyramidal path of the left side and by way of the corpus callosum with the pyramidal path of the right side This is the executive outgoing path for speech movements and a complete lesion of this path will result in inability to exteriorise spoken or written speech with relatively little impairment of comprehension of speech—the so called pure motor aphasia or pure agraphia Within the speech area of the brain thus limited little is known of any localisation of function but it is generally held that there is a gradual passing over from receptive functions (appreciation of spoken and written language) in the posterior regions to executive functions (exteriorisation of spoken and written language) in the anterior regions

In so far as the phenomena of word blindness and word deafness as well as motor aphasia and agraphia result from lesions of the speech area they seem to result from lesions of the tracts concerned rather than from damage to the cortex itself Lesions confined to the cortex and sparing the subcortical white matter unless they are extensive do not give rise to permanent disorder of speech

Physiological Considerations —Within a short time after birth the child begins to recognise the nature and uses of some of the objects in the world around it and to express its simple conscious processes by gestures and it early appreciates the gesture language of those around it The mimesis or gesture language thus early impressed and expressed remains throughout life the most stable the least vulnerable and the longest lasting of the methods of receiving and communicating ideas Long before it is able to utter any articulate sound the infant learns to connect certain sounds which it hears with certain objects and with certain events and the memories of these auditory patterns first implanted serve by far the most important function in the processes and expressions of thought throughout life Whereas we rely upon our visual memories for our remembrance and intelligence in general matters almost exclusively yet as regards speech we rely upon auditory memories to a very large extent and of course those who have never learned to read do so exclusively The process of recall both in silent thought and in speaking is the revival of auditory patterns From the original connection with hearing the memories of speech patterns come to be located in that part of the brain associated with the auditory function—in and around the temporal lobe Later guided by the auditory memories the child begins to express himself in articulate speech and he does so by the revival of auditory memories

All living motion is sense originated sense guided and sense governed and a motor process of itself has no proved conscious concomitant Our consciousness is that of the sensations which accompany the movement or which result from the movement The knowledge of correct execution so gained fortifies and increases the functional stability of the speech area and is of immense importance in the speech function If it be absent owing to a lesion isolating the speech area on the incoming side speech degenerates into a jargon and soon becomes impossible just as in tabes

the walking becomes irregular from loss of the muscular sense conveyed in the posterior columns and ultimately standing becomes impossible

When at a considerably later age the child learns to read and to write certain visual patterns (letters words sentences) become connected with certain objects and ideas, and become linked on to the already well established auditory memories of speech The meaning of the visual symbols is learned by the child from the meaning of the word or pattern spoken which he already knows well and the already developed auditory speech function serves as the instructor of the visual speech function and throughout life remains the more potent more dominant and less vulnerable function of the two

Later still in learning to write the child relies upon his visual memories, and *as his knowledge of correct execution in writing is largely visual and only in minor* degree common sensory from the movements of the hand in writing it follows that the function of exteriorising speech by writing becomes intimately connected with and a part of the visual speech function, and is usually depressed or lost with the visual speech function as the result of disease It will thus be seen that there are not separate regions of the speech area in which the auditory memories of language and the execution of spoken speech on the one hand and the visual memories of language and the execution of written language on the other hand are represented but that there are four functions intimately coupled in pairs which have their seat in the same anatomical substratum As has already been pointed out it is a general principle that when the speech area is damaged the speech function becomes depressed as a whole with the result that function is lost in order of its depth of impression

PATHOLOGICAL CONSIDERATIONS —By far the most common cause of aphasia in all its degrees and varieties is vascular disease Thrombosis accounts for the majority of these and embolism and hæmorrhage for the minority Trauma to the speech areas of the left hemisphere may cause a wide range of aphasic disturbances Cerebral tumour is the usual lesion causing aphasia of gradual onset and is much the commonest cause of jargon aphasia ' for there are few other lesions which can undercut and therefore isolate the temporal convolutions without otherwise interfering with their function

Left sided temporal lobe abscesses constantly cause aphasia as one of their early symptoms

Symptoms —Small lesions of the cortex seldom if ever produce lasting disturbances of speech This indicates that within the speech area there is no narrow localisation of cortical function and there must be capacity for compensation for such small lesions in the surrounding undamaged cortex With larger lesions of the cortex and in proportion to their extent mutilation of the patterns of speech slowness of utterance inability to find the words (inability to recall) especially nominals and above all isolated nominals occur in that order

In the *mutilated speech of the aphasic may* be sometimes noticed stammering This condition is at once distinguishable from true jargon aphasia since the former is slow and halting whereas the latter is facile and voluble Misplacement of words and the use of wrong words are common and are called ' paraphasia A tendency to repeat a word once pronounced is sometimes present and is designated perseveration of speech The same faults occur also in writing as faulty spelling misplacement of letters and words and the use of wrong words Much defect of general intelligence always accompanies severe damage to the speech area especially if comprehension of spoken speech is involved and this will be readily understood from the very large rôle which speech patterns play in the working of thought Difficulty in the recall of words and speech patterns which has been termed verbal amnesia ' or ' nominal deficiency is a characteristic feature of lesions of the speech area This difficulty is greater with spontaneous revival than with recall which is brought about by direct sensory stimulation For example an aphasic person who is unable

spontaneously to utter a word may repeat the word at once when it is spoken to him when he sees it in writing or when the corresponding object is shown to him It is important in this connection to bear in mind that we do not speak in the letters of the alphabet, nor in the words of our dictionary but in a running pattern of sound The pattern or context provides the meaning while the individual words are negligible and have no meaning The power of the pattern in aiding revival is very great both from sequence rhythm and musical quality As an example an aphasic who has no spontaneous utterance is told to count with his interlocutor The interlocutor begins counting the aphasic joins in The interlocutor then stops but the aphasic continues counting carried by the sequence rhythm

The confusional defects of speech function are met with in extensive damage to the speech area and are usual as immediate and transient phenomena in all suddenly occurring lesions of the speech area There is general mental dullness with varying degrees usually severe of depression of speech function and much confusion both on the acceptive and expressive sides when any of these functions remain and the results of the examination of the speech faculty are apt to vary very much from moment to moment for attention is very difficult to hold and the patient is easily fatigued and bored Severe degrees of this form of defect may be associated with inability to recognise objects— object blindness and with loss of ability to convey ideas by gesture— amimia

Prognosis —In attempting to estimate the degree of recovery which is likely to occur in cases of aphasia it is necessary first to bear in mind that sudden cerebral injury is apt at first by the process which has here been described as functional depression or diaschisis to cause very wide loss of function though the lesion may not be very extensive A total aphasia for example is often the immediate result of a lesion of moderate size Such phenomena last usually not longer than a week and until they have passed off it is impossible to make a definite statement either as to the extent of the lesion or the likely degree of recovery Speech may be regained by two entirely separate processes—either by recovery of function in partly damaged and functionally depressed areas or by compensatory activity in the undamaged portions of the brain The possible recovery of function will depend upon the nature of the lesion and upon its extent It will be greater when a lesion may be judged to be one of pressure rather than of actual destruction if such pressure be removable as in subdural hæmorrhage abscess and gumma and least when widely spread arterial disease and a failing heart suggest that the lesion is a thrombosis or when an irremovable tumour is present The greater the extent of the lesion if it be presumably from vascular occlusion as judged by the associated signs paralysis anæsthesia and hemianopia the less is the chance for functional restitution as there is then little hope of any useful restoration of the circulation through collateral vessels In children under the age of 6 years unilateral lesions produce no permanent speech defects provided sufficient intelligence remains but even to this rule some important striking exceptions have been recorded When adult life is reached transference seems to occur but little yet in a few recorded instances destruction of the posterior half of the speech area has been followed by an almost complete restoration of speech function

Treatment —The recovery of speech after a lesion causing dysphasia has much in common with the original acquisition of speech in a child The preservation of a certain degree of intelligence is essential to recovery and the younger the patient the greater the prospect of a successful outcome It is an unfortunate fact that the majority of cases of dysphasia occur in elderly subjects with arterial disease or in persons with infiltrating tumours in whom a gradual deterioration of cerebral function must be expected The most hopeful group are the young adults and children suffering from traumatic lesions of the brain or such transient cerebral lesions as subdural hæmatomas cerebral abscesses angiomatous malformations and benign tumours In such

cases spontaneous recovery of speech occurs gradually but it can be accelerated by a careful and patient system of re education at the hands of a speech therapist carried out either individually, or in groups

METHOD OF EXAMINATION —In examining a dysphasic person certain principles must be kept constantly in mind The patient is always anxious and easily alarmed He fatigues readily and is abnormally emotional and distractable It thus follows that he should be examined *in a quiet and physically comfortable environment* should be treated with gentleness and should only be examined for short periods such as half an hour at any one time

It should be remembered that dysphasia like all manifestations of disordered *cortical function varies in severity and quality from hour to hour and almost from* minute to minute in response to such varied factors as attention, fatigue and general bodily well being

It follows that the best record of an examination of a dysphasic patient is an *objective and factual one* a statement of what the examiner said or did and what the patient said or did in reply

Before any detailed investigation is attempted certain facts should be established and when possible confirmed from a relative (1) Is the patient right or left handed and if the latter, did he write with the right hand ? (2) What was his state of education as regards reading writing and knowledge of foreign languages ? (3) Is he deaf ? If so to what extent ? (4) Is his sight good or bad ? Is there hemianopia ? (5) Can he understand pantomime or gesture and express his needs thereby ? (6) What is his state of consciousness ? (7) To what extent is propositional speech preserved and to what extent can he convey a narrative in words ? What defects are evident *e g* perseveration paraphasia or jargon utterances ? (8) Can he name objects seen both simple and familiar and unfamiliar ? (9) Can he obey spoken commands ? (10) Can he select correctly a test object from a number of them in respon e to the spoken word ? (11) Can he write spontaneously and to dictation and what mistakes does he make ? (12) Can he copy printed or written words ? (13) Can he obey written commands ? (14) Can he write figures and carry out simple arithmetic calculations ? (15) Can he understand the significance of pictures ? (16) Can he draw such simple objects as a bicycle a flower or the façade of a house

Having obtained some insight into the patient s speech defect in a preliminary survey it is essential to assess *the degree of mental deterioration (if any)* that is present by the battery of tests employed to investigate a case of organic dementia since dysphasia and global mental deterioration each in its way increases and distorts the severity of the other

TESTAMENTARY CAPACITY —*No rule can be laid down as to the capacity* of a person suffering from aphasic speech defects to exercise civil rights and to make a will and each case must be judged upon its merits The first and all important consideration is the degree of intelligence and when this is good it is essential for such capacity that *there should be some mode of cognition and of expression left* In cases of uncomplicated executive aphasia either for spoken or written speech there is complete civil capacity but when as usually happens the two conditions coexist though intelligence and the receptive side of speech may be but little impaired yet *the expressive side of speech is reduced to gesture* and extreme difficulty may be met in ascertaining the patient s wishes Defects in the comprehension of spoken and written speech interfere seriously with testamentary capacity and with capacity for exercising civil rights In such cases there is great loss both on the acceptive and on the expressive *sides of speech with confusion of memory* and impairment of intelligence Most satisfactory results have however many times been brought about in apparently hopeless cases by careful sympathetic and repeated procedures in which the properties to be bequeathed and the likely legatees are assembled before *the patient thus allowing* the testator to match the gift with the recipient The

proceedings should be conducted in the presence and under the direction of a physician thoroughly conversant with the subject of aphasia All concerned should bear two points in mind, the one being that the wishes of the testator must be paramount, and the other that an obviously just will is most difficult to upset in a court of law

DYSARTHRIA

The conversion of mentally formulated speech symbols into spoken language requires the correct use of several mechanisms concerned respectively with the production of the voice by the passage of a stream of air through the aperture between the vocal cords and the articulation of words by movements of the lips tongue palate and jaws To defects of speech dependant upon disorders of these executive processes the term dysarthria is applied The neuro muscular mechanisms responsible for these movements are built upon the same principles as those which control other highly co ordinated voluntary movements for example those of the hand Impulses originating in the appropriate areas of the cerebral cortex are transmitted through the pyramidal tracts to the lower motor neurones (in the case of speech the various bulbar nuclei) and from these a further relay of impulses proceeds through the various peripheral nerves to the muscles concerned As in other movements the co ordination of these impulses is dependant upon the simultaneous reception of afferent impulses from the muscles and organs themselves and upon the activity of the cerebellum and other subcortical centres We thus find that the varieties of dysarthria are strictly comparable with the disturbances of voluntary movement encountered in the limbs

As we have seen impulses from the executive areas of the speech cortex are trans mitted to the lower centres through both pyramidal tracts and in consequence speech disturbances do not result from unilateral lesions of the pyramidal tract in the centrum ovale or brain stem If however both pyramidal tracts are damaged as commonly occurs in diffuse vascular degeneration double hemiplegia degenerative lesions of the pyramidal system diplegia tumours of the brain stem and in advanced cases of disseminated sclerosis the characteristic disturbance known as *spastic dysarthria* results Here the speech is slow, stiff and laboured Words are squeezed out with great effort as if through a rigid mechanism and are poorly formed on account of the stiffness and paucity of movement of the lips tongue and palate This condition is often referred to as pseudo bulbar palsy (p 1443)

When the lower motor neurones subserving the speech mechanisms are bilaterally affected *flaccid or atrophic dysarthria* results The speech is slurred indistinct and often slightly nasal Labial and dental sounds are especially affected but the laboured character of spastic dysarthria is absent Atrophic dysarthria is met with in lesions of the medulla oblongata of all kinds in progressive muscular atrophy and in multiple lesions of the bulbar nerves such as peripheral neuritis Spastic and atrophic dysarthria are characteristically found in combination in those cases of motor neurone disease in which both pyramidal and lower motor neurones are undergoing decay Primary weakness of the articulatory muscles may result in dysarthria This is met with in myasthenia gravis where the muscles are subject to excessive fatiguability and in some cases of myopathy where there may be great weakness of the muscles of the lips and jaws

Ataxic dysarthria is most characteristically heard in cerebellar disease especially when both sides of the organ or its afferent and efferent pathways are damaged as in Friedreich s disease disseminated sclerosis cerebellar degeneration and exten sive vascular or neoplastic lesions of the cerebellum and pons In mild cases speech becomes slow and deliberate with faulty spacing and accentuation of syllables the

so called "scanning" or staccato speech so common in disseminated sclerosis When more severe speech becomes explosive some syllables being slurred and almost inaudible others being produced with a gush of uncontrolled sound This coarse form of cerebellar dysarthria is most often met with in Friedreich s disease and in acute vascular lesions of the cerebellum and brain stem Dysarthria resulting from loss of afferent impulses from the periphery is rare but is occasionally met with in severe cases of peripheral neuritis and of tabes Conditions associated with involuntary movements may result in severe speech disturbance This variety of dysarthria is most commonly met with in cases of chorea and athetosis but may occur in other varieties of striatal disease, or as a sequela of encephalitis lethargica In Wilson s disease (p 1484) dysarthria results from muscular rigidity and goes on to complete anarthria A very characteristic variety of dysarthria occurs in general paresis, speech is slow and slurred and tremulous and there is a tendency to repeat or reverse the order of the syllables in polysyllabic words A very similar disorder may be met with in cases of chronic alcoholism and in some varieties of drug intoxication especially barbiturate poisoning

OTHER DEFECTS OF SPEECH

STAMMERING OR STUTTERING

A spasmodic defect of articulation leading to a sudden check in the utterance of words or to a rapid repetition of the consonantal sounds in connection with which the difficulty arises To the trouble of articulation are often added spasmodic movements of face and head or indeed of any part of the body

Except in the rarest instances this condition is not associated with any structural change in the nervous system or in the organs of articulation, but it has been observed as the end result of a lesion of the speech areas It occurs with a greater frequency than can be attributed to coincidence in naturally left handed persons who have been trained to behave as if they were right handed It not infrequently occurs in more than one member of a family but whether this implies a hereditary or environmental influence is uncertain as it may equally be acquired by a susceptible subject from other members of a child group The stammerer usually manifests one or other of a number of signs of incipient psychoneurotic instability such as abnormal timidity and excitability nocturnal enuresis night terrors and habit spasms, and though these symptoms may recede or disappear with time the stammerer remains more liable than normal individuals to develop neurotic manifestations under circumstances of stress

The disorder seems to consist of a lowering of the functional stability of the executive mechanism of speech by the effect of embarrassment either at a conscious or unconscious level It is begotten of shyness and self consciousness and probably for this reason is infinitely commoner in boys than in girls for the latter are much less liable to self consciousness It is never present in infancy or very early childhood but arises at the age when shyness and self consciousness first manifest themselves Its onset not uncommonly follows a debilitating illness such as measles diphtheria or whooping cough and it often appears after a sudden fright or an experience causing severe emotional strain or embarrassment Indeed it is the historical utterance of fright and of those who find themselves suddenly *in flagrante delictu*

Like other manifestations of anxiety in childhood it is more likely to occur in homes where there are disturbing factors such as parental discord favouritism and jealousy over indulgence or over strictness and frequent changes of teachers and surroundings

The stammerer never stammers in the speech of thought nor when talking aloud to himself alone nor at any time when singing for in the two former cases the embarrassment of self consciousness is absent and in the last case the element of rhythm and music greatly increases the stability and confidence of the function of speech In rebellious cases this element of self consciousness as well as the more overt evidences of psychological instability may gradually disappear while the stammer remains unaltered as an ineradicable habit

In articulate speech three muscular mechanisms are concerned (1) the respiratory mechanism for supplying the blast of air (2) the larynx for producing the voice and (3) the muscles of the lips tongue jaw and palate for articulation For distinct speech there must be absolute co ordination of these mechanisms one with another Consonants are in nearly all cases the source of the difficulty in stammering and while these are buccal sounds yet some begin with a laryngeal sound while others are purely buccal The former are termed ' voiced consonants ' and are B W V Zh Z Th (as in thus) D L R G Y and the latter ' voiceless consonants and are P F Th (as in thin) S Sh T, K while N M and Ng terminal are voiced nasal resonants ' If one articulates these consonants it becomes at once clear and it is the presence of the initial laryngeal element or voicing which makes the difference between B V Z D G and P F S T K respectively

A careful attention to the manner in which the letter sounds are produced is absolutely essential in the investigation and treatment of stammering The difficulty occurs most commonly with the explosive consonants P B T D G K and nearly always where these occur as initial letters—that is in starting the articulatory mechanism and to avoid this difficulty which arises after every pause most stammerers speak in a rapid monotonous fashion The fault chiefly lies in the direction of energy to articulation rather than to phonation The patient held up by his stammer usually remains silent but occasionally having produced the first sound he continues to repeat it—the reduplication stammer which has been the origin for the names stammer or stutter by which the malady is known Often the patient uses a trick or contortion to prevent the stutter or to relieve the feeling of nervous tension and embarrassment in consciousness which the defect causes and these tend to become engrafted on him as (1) associated sounds—whooping grunting crowing etc (2) habit spasms—contortions of the face limbs or body which sometimes take a complicated form and exactly resemble the co ordinated form of tic

Prognosis —The majority of the cases tend to a spontaneous cure and recovery is hastened in all cases by systematic treatment In every class of case the results of treatment may come slowly at first but perseverance will in almost every case bring success

Treatment —Attention should be paid to conditions of general health and to the mental well being and satisfaction of the child with plenty of scope for pleasure and for satisfying occupation When possible defects in the home and school environment should be eliminated Speech training at the hands of a trained speech therapist either individually or preferably in special classes is invaluable It is well for the patient to speak, read or recite in a large room alone loudly slowly and distinctly The following system for such exercises is useful (1) The chest must be kept well filled with air This most important point is often most difficult to the patient. (2) He must speak slowly with a full resonant voice (3) When he comes to the word on which he tends to stutter he should raise his voice and direct his energies to vocalisation and not to articulation If the difficulty be over a voiced consonant, he must be directed to voice it firmly If the consonant over which he stumbles be a voiceless one attention must be directed to the vocalisation of the subsequent vowel sound for instance in pat he must attempt to vocalise the at and he will find little difficulty in prefixing p as the syllable is uttered (4) Gymnastic and singing exercises are valuable additions to treatment Should associated movements be

so called 'scanning' or 'staccato' speech so common in disseminated sclerosis. When more severe speech becomes 'explosive', some syllables being slurred and almost inaudible others being produced with a gush of uncontrolled sound. This coarse form of cerebellar dysarthria is most often met with in Friedreich's disease and in *acute vascular lesions of the cerebellum and brain stem*. *Dysarthria resulting* from loss of afferent impulses from the periphery is rare but is occasionally met with in severe cases of peripheral neuritis and of tabes. Conditions associated with involuntary movements may result in severe speech disturbance. This variety of dysarthria is most commonly met with in cases of chorea and athetosis but may *occur in other varieties of striatal disease* or as a sequela of encephalitis lethargica. In Wilson's disease (p. 1484) dysarthria results from muscular rigidity and goes on to complete anarthria. A very characteristic variety of dysarthria occurs in general paresis; speech is slow and slurred and tremulous and there is a tendency to repeat or reverse the order of the syllables in polysyllabic words. A very similar disorder may be met with in cases of chronic alcoholism and in some varieties of drug intoxication, especially barbiturate poisoning.

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If with the lumbar puncture needle and manometer in position the right jugular vein is firmly compressed an immediate rise in the level of the fluid in the manometer will be noted in the normal person the pressure rising rapidly from the normal 80 to 120 mm to 300 mm or more On releasing the compression of the jugular the pressure rapidly returns to its former level If there is any block in the spinal subarachnoid space such as may be caused by extradural compression or a spinal tumour or if there is interference with the escape of fluid from the cranial cavity there will be no rise in the pressure of the lumbar fluid on jugular compression (complete block) or a rise of only a few cms (incomplete block) In the latter case release of the jugular compression will be followed by a very slow return of the meniscus to the former level or the level may remain unaltered indicating a ball valve type of obstruction Again if the withdrawal of a small quantity (4 to 8 ml) of fluid is followed by a persistent fall in the pressure of about 50 per cent there is probably obstruction to the normal flow of cerebrospinal fluid These two tests afford valuable evidence of any occlusion of the spinal subarachnoid space

Appearance of the Cerebrospinal Fluid —Any departure from the normal watery appearance of the cerebrospinal fluid is readily detected The fluid may be freely blood stained in cases of recent subarachnoid or cerebral hæmorrhage or of trauma to the brain In such cases the blood is usually present in large amounts and is intimately mixed with the cerebrospinal fluid in all specimens removed Blood contamination resulting from faulty technique in withdrawing the fluid can usually be recognised as it is usually scanty in amount and varies in intensity in different specimens If the blood has been mixed with the fluid for more than a few hours before withdrawal it assumes a slightly orange tint on account of the break down of the blood pigment Such a specimen if centrifuged or allowed to stand will give a bright canary yellow supernatant fluid a condition known as *Xanthochromia* In cases punctured several days after a severe subarachnoid hæmorrhage the fluid may be thick and brownish orange in colour In addition to cases of resolving subarachnoid hæmorrhage xanthochromia may be present in cases of long standing spinal blockage subdural hæmorrhage some cases of polyneuritis and occasionally in cases of cerebral tumour It is often associated with a great increase in protein content of the fluid, which may thus undergo spontaneous clotting on withdrawal

The combination of xanthochromia with greatly increased protein content of the cerebrospinal fluid and evidence of spinal block is known as *Froin s syndrome* (*loculation syndrome*) and is very characteristic of severe spinal compression

Turbidity of the cerebrospinal fluid is caused by the presence of a great excess of cells and is thus characteristic of meningitis It may vary in degree from slight opalescence to a frankly purulent fluid

Increase of Protein Content —This is of great importance and occurs in many pathological conditions of the central nervous system As has already been stated it may result from occlusion of the subarachnoid space from any form of spinal block It occurs in all cases of meningitis whether pyogenic, tuberculous or syphilitic It is one of the earliest changes in the fluid in cases of cerebral abscess It may be found in acute poliomyelitis and most virus diseases of the nervous system but it is slight or absent in encephalitis lethargica An isolated increase in protein content occurs in many cases of intracranial tumour particularly where the tumour impinges upon the surface of the brain or the walls of the ventricles It may be met with after vascular lesions of the brain even though there has been no escape of blood into the subarachnoid space and also in cases of acute infective polyneuritis

Increase in Cell Content —An increase in the cell count of the cerebrospinal fluid is found in almost all inflammatory diseases of the nervous system In pyogenic meningitis an enormous excess of cells is the rule and the vast proportion of the cells are polymorphonuclear leucocytes A small number of lymphocytes may also be present and the proportion of these gradually increases as recovery takes place A

The normal cerebrospinal fluid is a clear colourless fluid indistinguishable in appearance from water and it has a remarkably constant composition As obtained by lumbar puncture it contains from 0 to 5 cells (endothelial cells and lymphocytes) per c mm Its chemical composition is as follows

Protein (mainly albumin)	0 02 to 0 04 per cent	(20 to 40 mg per 100 ml)
Glucose	0 05 to 0 09 ,,	*(50 to 90 mg per 100 ml)*
Chlorides (as NaCl)	0 72 to 0 75 ,,	(720 to 750 mg per 100 ml)

In health the globulin content is insufficient to give a positive Nonne Apelt or *Pandy test*

LUMBAR PUNCTURE

The method by which the cerebrospinal fluid is best withdrawn for diagnostic or therapeutic purposes is by lumbar puncture The patient should lie in the left lateral position with the head supported by one pillow and at the same level as the lumbar spine A firm couch or operating table is to be preferred and if the operation is performed on the patient s bed the introduction of fracture boards under the mattress is advisable The patient s back must be in a vertical plane The knees are drawn well up to produce the maximum convexity of the spine, but the neck should not be sharply flexed *or pressure measurements will be inaccurate* The site of lumbar puncture is the midline in the interspace between the third and fourth or the fourth and fifth lumbar spines The skin should be anæsthetised with local anæsthetic and the lumbar puncture needle should be introduced accurately at right angles both to the longitudinal and transverse axes Pointing the needle even slightly upwards downwards or towards the side is likely to result in contamination of the fluid with traces of blood The whole procedure must be carried out with the utmost *attention to asepsis, and the precautions taken should not be less than those necessary* for a major surgical operation The needle thus introduced will be felt to penetrate in turn the spinous ligament and the dura mater and on withdrawing the stilette the fluid will flow freely in the normal subject at the rate of about 3 drops a second In the rare cases where lumbar puncture is impossible or inadvisable cerebrospinal fluid may be obtained either by cisternal puncture or by direct tapping of the cerebral ventricles

Pressure of the Cerebrospinal Fluid —This can only be ascertained by actual measurement with a manometer, estimates based upon the rate of flow are fallacious When it is necessary to measure the pressure a three way needle with manometer attachment should be employed and before the readings are taken the patient must be lying relaxed and comfortable with easy respirations The normal pressure of cerebrospinal fluid varies from 60 to 150 mm and will be seen to rise and fall over a distance of 5 to 10 mm with the respiratory movements Coughing and straining give rise *to an abrupt increase in the pressure of from 30 to 50 mm* A pressure of over 150 mm is evidence of increased intracranial pressure and readings of over 300 mm are common in the presence of intracranial tumours meningitis and other conditions characterised by raised intracranial pressure When the cerebrospinal pressure is found to be 300 mm or more fluid should be withdrawn slowly and in the minimum quantity necessary for pathological investigation (5 ml) as the rapid withdrawal of a large quantity of fluid may result in sudden death from the formation of a medullary pressure *cone or from uncinate herniation*

Queckenstedt s Phenomenon —In the normal subject the pre sure of the fluid in the lumbar sac directly reflects the pressure within the cerebral subarachnoid spaces and the ventricles and any change in the intracranial pressure is immediately transmitted through the patent subarachnoid space and causes a change *in the level* of the fluid in the manometer This forms the basis of the valuable test for patency of the subarachnoid space known as Queckenstedt s test

this relation exists the blow on the head has simply served to bring a pre existing tumour into symptomatic prominence by causing either œdema or hæmorrhage in its substance or vicinity It must be remembered in this connection that a cerebral tumour may exist for a long period without definite symptoms

Pathology —The pathological classification of intracranial tumours has a practical importance for when the nature of a new growth can be determined clinically some idea of its future behaviour can be formed and the surgeon can make his plans to meet the problems which each variety of tumour presents

The chief varieties of intracranial tumour are as follows

Tumour of the brain substance—Glioma
Tumour arising in the meninges or nerve sheaths {Meningioma / Neurofibroma}
Secondary carcinoma and sarcoma
Blood vessel tumours
Tumour of the pituitary body and stalk
Infective granuloma—Tuberculoma Syphiloma
Parasitic and other cysts

It is not possible to indicate with precision the relative incidence of these different types of tumour for the figures available from different institutions must reflect their particular circumstances and are not representative of the population as a whole But it is possible to state that glioma constitutes about 40 per cent of all intracranial tumours and meningeal and pituitary tumours together from 20 to 30 per cent Formerly the incidence of secondary carcinoma was said to be about 6 per cent but recent evidence has indicated that it is much higher and may well be as high as 20 per cent. of the total There can be no doubt that as greater precision in diagnosis is reached the frequency of this complication of visceral carcinoma becomes more fully recognised

GLIOMA —As its name implies the glioma is a tumour arising in the glial or supporting tissue of the brain but within the limits of this term are included growths of very varied cytological type and modes of growth Some are richly cellular highly vascular and rapidly growing others are relatively acellular and may be exceedingly slow in growth But they have certain important characteristics in common They originate within the substance of the nervous system and all infiltrate to a greater or less extent the surrounding nerve tissue They are thus invariably locally malignant They do not invade tissue outside the nervous system or cause metastases in other parts of the body though in some fragments may become detached and be carried in the cerebrospinal fluid to distant parts of the subarachnoid space and there continue their growth as distinct implantation tumours Gliomas are prone to undergo degeneration and necrosis If this is rapid it may lead to cyst formation if it is slow it may lead to calcification within the tumour Hæmorrhages into the substance of a glioma are common and the surrounding brain tissue is often œdematous Occasionally gliomas are multiple

Many types of glioma have been described but these classifications are ephemeral and largely artificial for more than one pathological type may be represented within a single tumour and the same tumour may present different features at successive periods of its course But with this reservation it is useful to recognise certain common and relatively well defined clinical and pathological types

Astrocytoma is the commonest of all gliomas and is a diffusely infiltrative tumour of the white matter which occurs at all ages and in any part of the brain Its structure is relatively uniform and its growth often very slow The survival period after local removal may be long especially when as in the cerebellum a satisfactory excision of the surrounding tissue can be achieved

lymphocytosis is characteristic of tuberculous and syphilitic meningitis and of most virus infections of the nervous system In tuberculous meningitis a mixed cytosis often occurs at first with as high a proportion as 40 per cent of polymorphonuclear cells, but as the disease progresses the proportion of lymphocytes steadily rises until they represent 90 per cent or more of the total cell count A mixed pleocytosis is also seen in cases of cerebral and extradural abscess, in sinus thrombosis and after extensive cerebral softenings

Decrease in Glucose Content —The glucose content of the cerebro spinal fluid is decreased in varieties of meningitis particularly in those due to pyogenic organisms in which case the fluid commonly fails to reduce Fehling s solution on boiling It is almost invariably reduced in tuberculous meningitis but only rarely in meningitis due to viruses (see p 1396) It is also reduced in some cases of neurosyphilis

Alteration of Chloride Content —The chloride content of the cerebrospinal fluid is lowered in all cases of purulent or tuberculous meningitis largely as a result of the diminution of the plasma chlorides, which occurs in these as in other acute febrile illnesses This change is of particular value in the diagnosis of tuberculous meningitis in which affection levels as low as 600 to 650 mg per cent may be found early in the disease in contrast to the relatively normal chloride content in the case of other diseases causing a lymphocytic pleocytosis

An increase in the chloride content as well as that of non protein nitrogen is found in uræmia and other conditions of salt retention

Lange s Colloidal Gold Reaction —In neurosyphilis and in some cases of disseminated sclerosis the globulin fraction of the total protein of the cerebrospinal fluid increases and may almost equal the albumin fraction The high globulin content gives the fluid a power of precipitating colloids from suspension The estimation of this power in relation to colloidal gold is the basis of Lange s test To 10 dilutions of cerebrospinal fluid (from 1 in 10 to 1 in 10 000) constant amounts of colloidal gold are added and the mixtures allowed to stand for 24 hours The form of the precipitation curves has a differentiating value Thus in general paralysis the first 6 dilutions are precipitated (paretic curve) in tabes dorsalis the third and fourth dilutions show the maximal precipitation (luetic curve) in meningitis the sixth to eighth dilutions are precipitated (meningitic curve) In disseminated sclerosis the combination of negative Wassermann reactions in blood and fluid and a paretic curve in the fluid is frequently found

Organisms —The nature of the organismal content is determined (1) by the direct examination of films made from the centrifugalised fluid (2) by cultures from the fluid and (3) by the inoculation of animals with the fluid

The Wassermann Reaction —This is positive in all conditions of recent syphilitic disease impinging upon the meninges and always in general paralysis Though often positive in tabes it may be found negative

INTRACRANIAL TUMOURS

Under this heading are grouped all new formations which encroach upon the intracranial space and which produce the familiar pressure symptoms and local symptoms of tumour though some of them are not strictly speaking neoplasms

Ætiology —The brain is one of the commonest seats of new growth in the body Further new growth is one of the commonest forms of structural disease of the brain—second only in incidence to lesions of vascular origin

Cerebral tumour may occur at any age but it is relatively rare in the very young and in the very old There is no significant difference in its incidence in the two sexes The relation between head injury and the first symptoms of cerebral tumour is one that has often been pointed out though it is likely that in most cases where

occur in the cerebellum and give rise to blood cysts They may be associated with similar tumours in the retina and may be familial—a combination often known as Lindau s disease

PITUITARY TUMOURS —These arise from the glandular elements of the pars anterior They usually take the form of an adenoma and may be composed of any of the three types of cell found in this body

The commonest is the chromophobe (neutrophil) adenoma consisting of a mass of neutrophil cells with clear vesicular nuclei lying in masses in a fine connective tissue stroma or occasionally arranged in columns or in a primitive alveolar formation This type of tumour is associated with symptoms of hypopituitarism The less common variety is composed chiefly of cells of acidophil type whose cytoplasm contains acidophil granules of varying size This type is associated with the clinical picture of acromegaly Both the foregoing varieties of adenoma commonly attain a sufficient size to expand the sella turcica and to escape from it to cause neighbourhood symptoms by involving the optic chiasma or the oculomotor nerves The rarest type of adenoma is that composed of cells containing coarse or fine basophil granules—the basophil adenoma associated with Cushing's syndrome This is a tumour of small size which may only be detected by making serial sections and never causes expansion of the sella or symptoms of involvement of neighbouring structures Very rarely pituitary adenomata may undergo malignant degeneration, and occasional examples of tumours of mixed cell type are met with

Another tumour arising in association with the pituitary body is the Rathke pouch or supra sellar cyst (adamantinoma) This arises from cell rests derived from the buccal outgrowth (Rathke s pouch) from which the anterior lobe of the pituitary is developed Such tumours are commonly situated above the sella turcica but may be partially or wholly intra sellar They are partially solid partially cystic tumours composed of masses of transitional epithelium lying in a fine connective tissue stroma and containing cystic spaces They frequently undergo degeneration and subsequent calcification and may reach the size of a golf ball and so come to protrude far into the floor of the third ventricle and obstruct its cavity so producing a severe degree of hydrocephalus

CHOLESTEATOMATA —These sometimes called mother of pearl tumours on account of their glistening appearance are found in connection with the basal meninges Their origin is uncertain They are of slow growth and may run a symptomless course They consist of a greasy greyish friable and more or less laminated mass made up of layers of a closely packed mosaic of flat polygonal cells The tissue is necrotic and contains no blood vessels

Among the rarer tumours of the brain may be mentioned dermoid tumours teratomata chordomata, which arise from rests of the anterior end of the primitive notochord and are found below the base of the brain lipomata fibromata neuromata neuroblastomata consisting actually of undifferentiated nerve cells and enchondromata

CYSTS —Cysts of the following varieties may be met with on the surface or in the substance of the brain (1) Serous cysts of the arachnoid These may occur as part of a diffuse arachnoiditis or may occur alone without any known cause (2) Porencephalic cysts These commonly result from softening after embolism or thrombosis or severe brain injury in early childhood They may lose all trace of their origin and form thin walled cavities containing colourless fluid which often extend from the ependyma to the pia mater and involve the whole thickness of the pallium (3) Cysts derived from tumours—especially gliomata and secondary carcinomata The tumour giving rise to such a cyst may be extremely small and may appear as a small nodule in one part of the circumference Such cysts contain a highly albuminous fluid which is often yellow in colour (4) Blood cysts which are usually derived from highly vascular tumours but may follow trauma or intracerebral hæmorrhage from

Glioblastoma multiforme is a tumour only slightly less common than the astrocytoma but is far more cellular rapidly growing and varied in its histological appearance It is a tumour of the cerebral hemispheres, and although it may occur at any age is commonest in middle age or later and usually terminates life within a year of its first symptoms Because of its invasive nature it is of all gliomas the least amenable to surgical removal

Medulloblastoma is a highly cellular and rapidly growing tumour almost confined to the roof of the fourth ventricle and cerebellum It is commonly found in children and is in the form of glioma most often spread by implantation across the subarachnoid space

Other varieties of glioma are described in relation to the ependyma choroid plexus and oligodendroglia

MENINGIOMA OR ENDOTHELIOMA —This is a connective tissue tumour which grows from the endothelial cells of the arachnoid villi particularly where these penetrate the walls of the dural venous sinuses Meningiomas are therefore found in the neighbourhood of the venous sinuses especially the superior longitudinal the spheno parietal the petrosal and circular sinuses They do not invade the brain but compress and displace it and may become deeply embedded in it They may infiltrate the overlying bone which may become so thickened that a visible or palpable boss is present on the surface of the skull Meningiomas are highly vascular tumours, and large nutrient vessels may be present in the neighbouring skull and scalp Calcification in the substance of these tumours is common

NEUROFIBROMA —This also is a connective tissue tumour arising from the sheaths of the cranial nerves The vast majority grow from the sheath of the auditory nerve and constitute the common tumour of the lateral recess—the acoustic neurofibroma Occasionally they grow from the fifth or other cranial nerves The neurofibroma may be solitary or may appear as part of a generalised neurofibromatosis when it is often bilateral on the acoustic nerves It is a firm nodular tumour which gradually buries itself in the side of the brain stem and often erodes the bones of the internal auditory meatus It is usually of very slow growth but may undergo necrosis and cyst formation

SECONDARY CARCINOMA —As has already been indicated secondary carcinoma is probably more common than is generally realised It is a frequent event in lung cancer which forms the most important source of brain metastases and it is not uncommon for symptoms of secondary involvement of the brain to precede those of the primary growth in the lung

Indeed in all adult cases presenting the signs and symptoms of intracranial tumour the possibility of carcinomatous metastasis should be explored particularly in a patient who is losing weight or deteriorating rapidly

Other common sources of metastatic tumours are the breast prostate and gastro intestinal tract

Carcinomatous deposits are commonly blood borne and multiple and are liable to undergo necrosis and cyst formation and hæmorrhage

Rarely they may reach the brain by direct invasion from the naso pharynx In exceptional cases there may be a diffuse infiltration of the subarachnoid space with carcinoma and when it occurs alone this meningitis carcinomatosa may be very difficult to diagnose

BLOOD VESSEL TUMOURS —Tumours and congenital anomalies of the blood vessels are relatively common in the brain compared with other organs They take two principal forms (1) angiomatous malformations consisting either of arterio venous varices or telangiectases These are most often found in the hemispheres but may occur in the brain stem or cerebellum They involve the brain diffusely particularly on its surface and may present themselves as tumours or as cases of cerebral hæmorrhage (2) True angiomatous neoplasms or hæmangioblastomas which commonly

is thus favourably placed to produce internal hydrocephalus In elderly persons on the other hand the picture of a tumour is apt to be blurred general signs are late in development and focal signs are indistinct Possibly the presence of a background of cerebral arterial degeneration and its associated cerebral changes are responsible for this blurring of clinical outline It may be supposed that the tumour does not write its mark upon a clean slate when arterial and cerebral degeneration are already present

GENERAL MANIFESTATIONS —These symptoms are the result of an increase in intracranial pressure and are therefore absent in cases of tumour where the pressure remains normal The degree to which a cerebral tumour causes an increase in intra cranial tension is very variable and depends upon a number of factors The growing tumour by its bulk occupies a portion of the available intracranial space which is a constant and therefore after displacing cerebrospinal fluid the tumour causes directly a rise in pressure Many tumours from their position interfere with the free flow of fluid through the ventricular system and thus produce an obstructive hydrocephalus This accounts for the rapid increase of pressure seen in tumours of the cerebellum mid brain and third and fourth ventricles Other tumours may interfere with the normal venous return from the hemispheres and so produce œdema of the brain tissue with a proportionate increase in its bulk These different factors often reinforce one another and thus set up a complex vicious circle This in large measure explains the undoubted fact that a given tumour of rapid growth gives rise to much greater increase in intracranial pressure than does one of similar size and position which has developed slowly

The general manifestations of increased intracranial pressure consist of the following papillœdema headache vomiting mental drowsiness and loss of vivacity double vision alterations in the pulse rate blood pressure and respiration giddiness nasal irritation and occasionally generalised convulsion

Papillœdema —This is by far the most constantly present of all the general manifestations Papillœdema appears to be a stasis œdema of the nerve head owing to the increased intracranial pressure forcing the cerebro spinal fluid into the meningeal sheath which invests the optic nerve and into the perivascular spaces which accompany the central vessels of the nerve The nerve sheath becomes distended and venous stasis occurs On ophthalmoscopic examination the earliest changes are increased redness of the disk with disappearance of the physiological pit As the process increases the whole margin of the disk becomes lost It enlarges in area and becomes visibly swollen and presents the appearance of a mole hill as seen from above The point of emergence of the vessels at the centre of the disk becomes buried by white exudation which occurs also all over the disk and taking a form determined by the radiating nerve fibrils gives the disk the appearance of being striated in a radial fashion like a chrysanthemum A similar exudate may rupture the membrana limitans interna in little droplets at the macula and coagulating as it comes in contact with the vitreous humour produces the *characteristic radially* arranged macular figure or macular fan exactly similar to that seen in renal disease The venous congestion of the retina leads to multiple hæmorrhages which infiltrate along the radially arranged nerve fibres and for this reason are flame shaped With the outpouring of much exudation, the disk becomes white In the course of time the hæmorrhages become white flame shaped scars the whole disk contracts the swelling disappears and the disk becomes white flat and atrophic and distinguished only from that of primary optic atrophy by the scarred remains of the exudate at its edge producing a fluffy outline like that of torn cotton wool along the vessels and at the centre In the early stages of papillœdema even though there be considerable swelling of the disk vision is little impaired As the process increases however in proportion to the degree of the swelling to the amount of exudate and to the length of time the papillœdema has lasted consecutive optic atrophy sets in

any cause (5) Cysts following the breakdown of areas of the brain which have become necrotic from vascular occlusion (6) Cysts of the septum pellucidum (7) Colloid cysts of the third ventricle (8) Cysts derived from remnants of the developing pituitary body and described in connection with pituitary tumours (9) Dermoid cysts (10) Parasitic cysts of which the more common is the bladder worm of the tapeworm, tænia solium which is called on account of the thickness of its wall, cysticercus cellulosæ These are usually multiple, and grow in the folds of the pia mater in the depths of the sulci and occasionally in the fourth ventricle It is usual for these cysts to shrink and become calcified in from 3 to 6 years Less commonly the hydatid or cyst of tænia echinococcus is found It is usually single may reach a large size and present the signs of a slowly growing tumour with eosinophilia

INFECTIOUS GRANULOMATA —Tuberculomata are more common in the young but they may occur at any age They are secondary to tuberculosis elsewhere in the body They vary in size from that of a grain of wheat to that of a pigeon s egg and are more often found in the cerebellum and brain stem than in the cerebral hemispheres They may be solitary or multiple When large, caseation occurs in the centre and on section the tumour presents a dry yellowish crumbling or even diffluent centre with a greyish red peripheral growing zone where are located living tubercle bacilli and actively growing tubercles In old tuberculomata very dense calcification may take place with the formation of so called brain stones ' Before the advent of antibiotics the surgical removal of tuberculomata although readily carried out, was associated with so great a risk of fatal tuberculous meningitis that it was best avoided Now this risk can to a great extent be controlled and surgical removal is often the treatment of choice of chronic tuberculomata

Syphiloma is to day a very rare intracranial tumour It grows most often from the meninges and is thus a surface tumour though it may burrow deeply into the brain tissue It is most commonly found above the tentorium It is occasionally very hard in consistency and tends in many cases to scar and become obsolete It is sometimes impossible to distinguish this tumour from a tuberculoma without the aid of a microscope and the serum reaction Actinomycetoma and tumours from other streptothrix infections are also rare

Symptoms —The rates of growth of the different kinds of tumour vary widely Some cases run their course from onset of symptoms to fatal termination within a few weeks while in others there is evidence of gradual growth over a period of years In the latter group it may be only in the final stage that the true nature of the illness becomes apparent, and only in retrospect that earlier symptoms assume their real significance This is especially so in the case of those tumours which for months or years have manifested their presence only by generalised epileptiform fits In yet other cases an intracranial tumour may remain latent during life being revealed unexpectedly at post mortem examination

Between these two extremes a great variety of symptom complexes may be presented by an intracranial tumour Thus it may first show itself by producing signs of raised intracranial tension alone—that is by general signs or by signs of a gradually progressive *local* lesion alone—that is by *focal* signs *Whichever of these two elements* is initially lacking will probably appear later A third manner in which a tumour may first signal its existence is—as has been mentioned—by the occurrence of generalised epileptiform fits in the absence of any other symptoms and signs In this instance also general and focal signs will probably ultimately make their appearance Again a sudden onset of symptoms from hæmorrhage into a glioma or from œdema of surrounding brain may usher in the clinical course of a tumour within the skull

The age of the patient is not without influence in determining the symptomatology and clinical course of a tumour Thus in childhood the early appearance of greatly raised intracranial tension—that is of general symptoms is the rule This is mainly due to the fact that at this age the tumour is commonly in the fourth ventricle and

a slight heaviness and an absence of restlessness which is of value in diagnosis It is almost unheard of for a tumour patient to suffer from insomnia As the symptoms increase so do heaviness and drowsiness though a perfect but slow cerebration may persist until the latest stages of the disease

DIFFERENTIAL DIAGNOSIS OF TUMOURS IN THE PITUITARY REGION (WALSHE) (MODIFIED)

	Adenoma			Pituitary Stalk Tumour	Meningioma	Glioma of Optic Chiasma (rare)
	Chromophobe	Chromophil	Mixed Cell			
Age Incidence	From adolescence onwards			From 10 years to early adult life	From 30 years onwards	Usually in childhood
Fundus Oculi	Primary optic atrophy			Papillœdema in children usually primary optic atrophy in adults	Primary optic atrophy	Primary optic atrophy
Visual Fields	Bitemporal hemianopia (——Occasionally homonymous hemianopia——)			Bitemporal hemianopia or central scotomata	Bitemporal hemianopia	Bitemporal hemianopia proceeding to early blindness
Pressure Symptoms	Absent or late			Early and severe except in adults	Absent or late	Absent or late
Glandular Symptoms	Hypopituitarism	Hyperpituit or Hypopituit	Mixed	Hypopituitarism	Nil	Nil
Situation	Sellar			Suprasellar	Suprasellar	Suprasellar
Radiological	General enlargement and deepening of sella			Shadows above and in sella Sella shallow and with uneven floor	Commonly no change	Enlargement of sella forwards beneath ant clinoid processes

Double vision —Diplopia is a common symptom and is usually at first intermittent and experienced on looking to one or both sides It is due to weakness of one or both external rectus muscles and may be associated with an obvious convergent squint

vision becomes impaired and blindness results Peripheral constriction of the visual fields large pupil and dimness of vision are the signs that if the papillœdema be not speedily relieved blindness will certainly result Perfect vision may be retained for a time even with a high degree of papillœdema So important is papillœdema in the diagnosis of tumour of the brain that it is necessary to bear constantly in mind all other causes which may give rise to it

Papillœdema may occur in certain general intracranial conditions other than tumour (1) In meningitis as a late sign rarely before the tenth day and as many *cases of meningitis do not last so long it is chiefly met with in the less acute forms* such as tuberculous meningitis (2) States of arterial hypertension from whatever cause but particularly in malignant hypertension in young subjects (3) Renal disease may give a retinal picture of intense papillœdema macular figure and hæmorrhages sometimes quite indistinguishable from that due to tumour This is often seen in the small white kidney of young subjects and sometimes in small red kidney but there is no form of renal disease in which papillœdema has not been observed (4) Anæmic states of various kinds sometimes give rise to papillœdema As regards groups (3) and (4) it is essential to emphasise the facts that papillœdema headache and vomiting may occur as a symptom complex both in renal disease and in anæmic states (5) Septicæmic conditions especially infective endocarditis may *cause papillœdema (6) Lastly, papillœdema has been noted in connection* with compression of the uppermost part of the cervical cord and with acute myelitis

The retinal changes in diabetes are always and those in renal disease often distinguishable from papillœdema resulting from increased intracranial pressure *In* diabetes the change is essentially a hæmorrhagic retinitis due to degeneration of vessels sometimes with waxy looking exudation in circinate patches and in renal disease it is often a general œdema of papilla and retina with hæmorrhages and white patches far away from the disk The papillœdema resulting from increased intra cranial pressure is always bilateral though it may appear in one eye before the other unless there be local pressure upon one optic nerve which always delays or prevents papillœdema appearing in that eye Otherwise an earlier commencement upon one *side is of no localising value*

Headache —The sensation may vary from a mere feeling of fullness of the head to the most agonising pain It is more often remittent than continuous and may be absent for long periods together *it often occurs on first waking in the morning* or after a period of recumbency or stooping It is rarely localised to any definite region except when the growth actually involves the bone or when pressure has caused local thinning of the bone when local pain and tenderness on pressure may *occur* Usually it is referred indefinitely to the frontal or to the occipital or to the vertical region When occipital it may be associated with pain and stiffness of the neck and head retraction This is due to a general pressure effect and does not indicate any localisation Headache may be entirely absent even in the presence of severe papill œdema It may precede the development of papillœdema even by a long period or may be later in its appearance

Vomiting —Only two thirds of all cases of intracranial tumour present vomiting as a symptom It rarely occurs in the absence of the two chief signs of increased intracranial pressure papillœdema and headache When the headaches are severe it may be associated with much nausea and the attacks are often referred to by the *patient as* bilious attacks Usually a result of increased pressure it may be directly produced by lesions of the cerebellum irritation of the vestibular nerve and the visual disorientation resulting from diplopia As a symptom of intracranial tumour *it hardly deserves the* cardinal importance which has been assigned to it in most descriptions of this disease

Loss of vivacity and mental drowsiness —Even when intellectual capacity shows not the slightest *impairment there* is from the first onset of symptoms a loss of vivacity,

fields and will in addition give rise to dilated pupils inactive to light Less severe degrees of papillœdema may give rise to irregular constrictions of the fields of vision, which may easily be mistaken for an incomplete bitemporal or homonymous hemianopia When intracranial hypertension is severe particularly in the case of posterior fossa tumours a considerable degree of deafness may be present due to congestion of the structures of the internal ear on one or both sides

Proptosis is by no means uncommon in tumours of rapid growth or in the presence of rapidly developing internal hydrocephalus It is caused by venous congestion of the orbital contents and may be more marked on one side than on the other In women amenorrhœa may occur in cases with tumours elsewhere than in the neighbourhood of the pituitary body It is particularly common in mid cerebellar tumours causing severe hydrocephalus

Especial mention may be made of tumours of the pituitary body and stalk Their signs consist of a combination of endocrine disturbance and symptoms due to damage of surrounding nerve structures and have been described in a previous section but since the tumours in this neighbourhood have their own typical symptom complexes the table as shown on p 1387 may be useful in differentiating them

Diagnosis—The differential diagnosis of intracranial tumour has to be made from (1) other conditions causing papillœdema (2) other conditions causing headache and (3) other local lesions causing symptoms and signs of local diseases of the brain

Renal disease arterial hypertension cerebral syphilis and rarely encephalitis may be characterised by all three groups of symptoms and so present peculiar difficulty and should be considered in every case of suspected cerebral tumour Cerebral abscess is in a special category since it is a tumour in the wider sense of an expanding intracranial lesion and so shares all the general and local features of tumour Abscesses nearly always follow obvious suppuration elsewhere especially in the middle ear or nasal sinuses or in the thorax but they may be latent for long periods Their onset is insidious but usually more rapid than in the case of tumour and general signs such as low fever a toxic appearance and changes in the cerebro spinal fluid are present (see p 1405) Other causes of obstructive internal hydrocephalus may closely simulate tumour of these chronic arachnoiditis stenosis of the aqueduct of Sylvius and syphilitic or other forms of chronic basal meningitis may be mentioned Saccular aneurysms of the larger cerebral blood vessels may be mistaken for tumours with disastrous results

The diagnosis of intracranial tumour is not complete when a decision is reached that such a lesion is present within the skull it is necessary to localise its position and if possible to determine its nature This topographical and pathological diagnosis calls for a skilful evaluation of the various symptoms and signs against the background of the patient s history Careful examination of the skull should never be omitted This may reveal asymmetry of contour thickening of bone dilated blood vessels or areas of tenderness or altered percussion note which may give valuable information Auscultation may reveal an audible bruit In experienced hands this purely clinical approach gives results of considerable precision in many cases but there will always be a number of cases in which a complete diagnosis cannot be reached by purely clinical methods In the majority of these it will be evident that a tumour is present but the evidence will be insufficient to determine its position and nature In a minority a local lesion may be diagnosed with certainty but there may be doubt whether it is a tumour or some other destructive lesion In either case recourse has to be made to instrumental aid Radiographs of the skull may give valuable assistance These may show changes indicative of long standing increased intracranial pressure areas of local absorption of bone abnormal vascular channels or areas of abnormal calcification Examination of the cerebro spinal fluid may give valuable information but it should be practised with caution if there is reason to *suspect much increase in intracranial pressure* and should be avoided in the presence

Blood pressure, pulse rate and respiration—In many cases of intracranial tumour of slow growth these functions remain unaltered until the terminal stage of the disease, but in cases where there has been an excessive and rapid rise in intracranial pressure *e g* rapidly growing or degenerating tumours abscess, or extradural and subdural hæmorrhages they may be considerably altered Fall in the pulse rate is the most constant change and may reach figures around 40 per minute in a person with a normal rhythm of 70 to 80 per min Less common is a rise in blood pressure occurring *pari passu* with the fall in pulse rate It is most often seen in cases of rapid cerebral compression and is characteristic of extradural hæmorrhage Respiration tends to be slow and shallow and when cerebral compression is severe it is often irregular and may become grouped and may show the wax and wane of movements which bears the name of Cheyne Stokes respiration When the respiratory function is depressed the lips and extremities may be cyanosed—a sign of ill omen in tumour cases

Giddiness—This symptom is not infrequently reported by patients with intra cranial tumour particularly if it is situated below the tentorium It usually consists of a feeling of faintness and general unsteadiness particularly on stooping but may amount to true vertigo

Nasal irritation—This curious symptom is seen sufficiently often to make it worthy of mention The cause is quite unknown

Convulsions—As will be stressed later epileptic fits of all types indistinguish ble from those of idiopathic epilepsy are among the commonest early symptoms of tumours originating above the tentorium Much more rarely they may occur as a symptom of general increase in intracranial pressure particularly in young children and in cases where the increase of pressure has been very abrupt

FOCAL SIGNS—These have been fully described in the section upon the local isation of lesions of the brain but certain points require further emphasis Of all the early symptoms of tumours above the tentorium the most common is the occur rence of epileptic fits These may take the form of focal fits of any kind or may be generalised and may precede any other manifestation of intracranial tumour by many years Any person developing fits for the first time after the age of 25 should be looked upon as a tumour suspect Although in all cases of intracranial tumour the symptoms and signs of raised intracranial pressure ultimately make their appearance they may be late in doing so and in such cases the clinical picture is that of a pro gressive local destruction of brain tissue

In examining cases of intracranial tumour signs may be observed which appear to be conflicting or mutually contradictory In such it should be remembered that symptoms and signs which appear early in the clinical course are of greater localising value than those which appear late and that signs which only make their appearance in the presence of a severe rise in intracranial pressure should be treated with great reserve Of these so called false localising signs the most notorious is the abducens paresis seen in most cases of raised intracranial pressure It probably results from shifting of the brain stem and stretching of the nerve in its course through the sub arachnoid space and should always be disregarded as a localising sign To a less extent the same is true of the third fifth and seventh pairs of cranial nerves whose functions may show slight impairment in the presence of greatly increased pressure without any direct involvement of their fibres in the tumour On the other hand cranial nerve palsies occurring early in the course of the disease before there is any increase in intracranial tension may be valuable evidence of direct involvement of these nerves either in the brain stem or in their courses through the subarachnoid space or foramina of exit

The presence of papillœdema may considerably modify the localising informa tion to be obtained through the function of vision Blindness will naturally destroy all information which might have been obtained from an examination of the visual

is often justified But it would be a mistake to suppose that surgical intervention is a matter of routine in every case in which intracranial tumour is diagnosed Each case must be considered on its merits

Failing the possibility of a successful removal the palliative operation of decompression may be needed to relieve the symptoms caused by raised intracranial tension This consists of the free removal of bone and the incising of the dura mater over the region of the tumour For brain stem tumours decompression is not only useless but also dangerous

In cases in which complete removal has proved impossible deep X ray therapy may be employed The results are very variable Some types of tumour notably the medullablastoma respond very favourably at the time but usually recur after an interval which grows longer decade by decade as radiotherapeutic technique improves A survival period of 10 years or more is now not uncommon The response in the case of astrocytomas and glioblastomas is much less predictable but on the whole, is disappointing and when improvement occurs it is short lived

Relief of pressure by dehydration —There are circumstances in which it may be desirable and necessary to reduce the brain volume and the intracranial pressure, for example to relieve pressure headache to avert impending coma or death to render the patient capable of co operating in his examination and thus facilitating a localising diagnosis and finally to make surgical procedures more easy This may be achieved by administering hypertonic solutions In the ordinary case the rectal injection of from 2 to 3 oz of magnesium sulphate dissolved in 8 oz of water may be tried But for a very rapid effect intravenous injection of from 50 to 75 ml of a 50 per cent. solution of dextrose or sucrose or of a 15 per cent solution of sodium chloride is effective It should be remembered that when the effect of such medical decompression has worn off the symptoms of raised intracranial pressure are apt to reassert themselves with increased severity These methods should therefore only be employed with restraint when there is only a short time to be tided over before surgical relief is available Pain and vomiting may be relieved with the various analgesics of the coal tar series Morphine should not be used as it is followed by grave depression of respiration Codeine phosphate is a valuable analgesic which is relatively free from this disadvantage

MENINGITIS

Definition —The inflammatory processes to which we apply the name of meningitis are infective in origin and usually have their seat in the leptomeninges—the pia arachnoid A true inflammatory lesion of the dura mater that is pachymeningitis is much less common and is usually a localised process due to the direct spread of infection from adjacent bone

Acute leptomeningitis on the other hand is usually generalised and even when it arises from a local focus of infection it spreads rapidly throughout the subarachnoid space this spread being facilitated by the cerebro spinal fluid and also by the negligible bactericidal potency of this fluid Further the inflammation not only produces its characteristic changes in the pia arachnoid but also greatly changes the composition of the cerebro spinal fluid These changes may be said to reflect with considerable accuracy the nature and cause of the meningitis and thus it is that the examination of this fluid has so great a diagnostic value Acute leptomeningitis may result from invasion of the leptomeninges by organisms carried in the blood stream as occurs in septicæmic conditions meningococcal meningitis tuberculous meningitis and many cases of pneumococcal meningitis Alternatively the organism may reach the meninges by direct spread from a neighbouring focus of infection of which suppuration in the middle ear and nasal sinuses infections of the scalp skull face and eye and cerebral

of more than a trace of papillœdema Manometry may establish the presence or absence of raised intracranial pressure and analysis of the fluid may thro v important light upon the nature of the pathological process in the brain But the most important acce sory methods of diagnosis are ventriculography and angiography Ventriculo graphy is a purely surgical procedure and should only be carried out by an experienced neuro surgeon under circumstances in which it is possible to proceed forthwith to a major cerebral operation, if this should prove necessary By ventriculography, not only can the localisation of a tumour in many cases be established with accuracy but its extent can be defined, thus enabling the surgeon to plan his operation to the best advantage Further a number of cases can be demonstrated to be inoperable thus sparing the patient the discomfort of a fruitless exploration As experience and skill in ventriculography increase it becomes increasingly obvious that in very few cases can this investigation be wisely omitted before an attempt is made to remove a brain tumour Cerebral angiography by which radiographs of the cerebral blood vessels are taken while they are filled with an opaque substance has a more limited but increasing value in the investigation of tumours of the cerebral hemispheres and is now almost essential in cases of vascular tumours and suspected aneurysms In some cases the electro encephalogram may afford evidence of localising value

Course and Prognosis —An intracranial tumour usually causes increasing symp toms which progress with exacerbations and remissions until papillœdema ends in blindness and until the pathological intracranial condition becomes incompatible with even a vegetative existence Death usually comes in one of two ways More commonly the patient sinks gradually into stupor and from this into deepening coma in which he dies from hypostatic broncho pneumonia In a minority of cases death occurs suddenly by an abrupt cessation of respiration The patient becomes deeply cyanosed for the heart continues to beat for many minutes after respiration has failed and in such a condition the patient may be kept alive for hours by artificial respiration This mode of death is most common when the increase of intracranial pressure has been great and of rapid development as occurs in many posterior fossa tumours It is attributable to the failure of the medullary centres from the forcing of the cerebellum and brain stem down into the foramen magnum or from pressure exerted on the mid brain by herniation of the uncus through the incisura of the tentorium This accident may readily be precipitated by withdrawal of cerebro-spinal fluid by the lumbar route and it is for this reason that great caution should be exercised in performing this operation on patients with high intracranial pressure Occasionally a tumour may become obsolete A tuberculoma may heal and ulti mately become calcified and a glioma may degenerate or cease to grow, but these events are too rare to be considered within the bounds of practical perspective The average duration of cases not operated upon rarely exceeds a year after diagnosis has become certain

Treatment —The natural termination of a case of intracranial tumour is death and the ideal of treatment must be the successful removal of the growth by surgical operation Failing this and it is frequently impossible all that can be hoped for is the relief of headache and sickness and delaying of blindness

In respect of the radical surgical treatment of tumours it will be remembered that probably more than half of the cases (if we include glioma and secondary carci noma) are infiltrative tumours in the brain substance and thus not amenable to com plete removal In such it is clearly improper to carry out mutilating operations which can at best only serve to prolong for a time a life which is a burden both to the patient and his relatives On the other hand signal successes can be obtained in the case of meningiomas tumours of the auditory nerve and the pituitary body and some cystic astrocytomas particularly of the cerebellum It will therefore be seen how important it is to be able to determine with some precision the nature of the tumour present in any given case When this is not possible an exploratory operation

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abscesses are the most common It may also gain direct access by penetrating wounds of the head and as a complication of fracture of the base of the skull

Pachymeningitis may be cranial or spinal and is usually secondary to either syphilis tuberculous disease of bone or middle ear suppuration The condition *formerly known as* pachymeningitis hæmorrhagica interna is now regarded as traumatic and not inflammatory in origin, and is described under the heading of chronic subdural hæmatoma (see p 1450)

The fine infiltration of the pia arachnoid by the cells of secondary carcinoma of glioma or sarcoma has been spoken of as a meningitis but although such an infiltration may give rise *to symptoms resembling those of a true meningitis the term is* not strictly accurate, though it is well to bear in mind that this form of new growth does occur and give a picture of meningeal irritation

The most useful classification of the varieties of meningitis is according to the nature of the micro organism producing the inflammation namely (1) Meningococcal Meningitis (2) *Pneumococcal Meningitis* (3) *Pyogenic Meningitis*, (4) Tuberculous Meningitis (5) Benign Lymphocytic Meningitis, (6) Syphilitic Meningitis and (7) Other Forms of Meningitis

(1) MENINGOCOCCAL MENINGITIS (see p 54)

(2) PNEUMOCOCCAL MENINGITIS

Ætiology —Pneumococcal infection of the meninges most commonly follows upon a similar infection elsewhere in the body empyema and pneumococcal otitis being the commonest lesions while pneumonia abdominal infection abscess and joint infection are less common In one third of the cases however the meningeal infection is primary The characteristics of the cerebro spinal fluid are that it is purulent and sometimes so thick that it will not flow through the needle It is greenish yellow in colour, contains a large amount of albumin and multitudinous polymorphonuclear cells, among which the characteristic pneumococcus is found In fulminant rapidly fatal cases the fluid may be turbid from the presence of pneumococci alone *no reaction in the form of pleocytosis being present The disease may occur at any* age It is sometimes a terminal event of a pneumococcal infection elsewhere and passes almost unnoticed or is discovered only at the autopsy Meningitis which follows operations upon the nose and disease of the nasal bones is usually of the pneumococcal variety

Pathology —The surface of the brain and spinal cord is highly characteristic Usually the whole surface of the vertex and of the base is covered with a thick tenacious greenish yellow pus which is contained in the meshes of the arachnoid and between this and the dura The ventricles often contain pus A similar exudation is found upon the spinal cord more especially upon the dorsal aspect and in the cervical and lumbo sacral regions The major affection of the vertex of the brain is the peculiarity of this disease and only in the rarest cases is the base alone affected The exudation is characterised by a greater amount of fibrin than in other forms of meningitis

Symptoms —The symptoms are those which are common to all forms of meningitis Some of the cases are indistinguishable symptomatically from those of tuberculous meningitis *Others run a very rapid course and present few features other* than headache vomiting and pyrexia with a rapidly oncoming and quickly fatal coma In others again the meningeal symptoms are concealed in the terminal asthenia of a previously existing pneumococcal infection elsewhere such as empyema purulent pericarditis or peritonitis

Diagnosis —This rests upon the presence of signs of meningitis or the existence of coma alone together with a cerebrospinal fluid which is purulent from the presence of polymorphonuclear leucocytes and the finding of pneumococci in the fluid

Prognosis and Treatment —In the past pneumococcal meningitis was uniformly fatal Occasional recovery was later reported as a result of treatment with pneumo coccal antisera

The introduction of sulphonamide therapy led to a marked improvement in the outlook and the use of penicillin has completely changed the prognosis in this grave disorder in which the mortality should not now be more than 10 to 20 per cent if treatment is initiated immediately According to Honor Smith and her co workers penicillin should be administered intrathecally by the lumbar route in doses of 8000 to 16 000 units 12 hourly for the first 2 days and thereafter 24 hourly for a further 3 days This should be combined with intramuscular administration of 120 000 units of penicillin daily and with sulphadiazine by mouth an initial dose of 4 g being followed by 2 g 4 hourly for several days after the fever has settled Adverse re actions have been reported in cases where more than 20 000 units of penicillin were administered intrathecally in one dose Blockage of the cerebral or spinal subarachnoid space by the accumulation of organising purulent lymph may necessitate the giving of penicillin by the cisternal or ventricular routes

More recently favourable results have followed the use of penicillin alone in massive doses intramuscularly 2 000 000 units every 2 hours, none being given intrathecally

(3) PYOGENIC MENINGITIS

Apart from meningococcal and pneumococcal infections suppurative meningitis may result from the invasion of the meninges by staphylococci streptococci gono cocci *H influenzæ* coliform bacilli *B anthracis* and streptothrix

Staphylococcal and streptococcal infections are by far the most common They may result in young children from septic conditions of the umbilicus and from infec tions of the skin Usually they are due to extension of an infection from structures adjacent to the meninges and follow disease of cranial and spinal bones, especially caries in the middle ear erysipelas and other infections of the scalp wounds of the meninges especially bullet wounds rupture of intracranial abscess and they may occur in the course of a general septicæmia

Pathology —The pathology of these conditions does not materially differ from that of pneumococcal meningitis In all cases the exudation is purulent and in the meningitis due to *B anthracis* it is of a red colour due to concomitant blood effusion The cerebro spinal fluid contains large numbers of polymorphonuclear leucocytes together with the micro organism responsible for each variety Suppurative menin gitis resulting from bone disease and from wounds of the meninges may be localised by the formation of meningeal adhesions and an intrameningeal abscess may result Such an abscess situated upon the upper surface of the temporal bone is not an uncommon result of caries of the middle ear

The clinical aspect is that common to all forms of acute meningitis high pyrexia rigors and delirium being conspicuous The course is rapid and before the intro duction of modern chemotherapy led to an almost invariably fatal termination In the localised form where drainage can be ensured and extension of the infection prevented recovery should take place

Diagnosis —This depends upon the presence of the clinical signs of meningitis and of a cerebro spinal fluid containing polymorphonuclear leucocytes in large quanti ties and upon the recognition in this fluid of the several micro organisms responsible by microscopic examination and culture The recognition of *H influenzæ* requires that cultures should be made upon a blood medium for otherwise the organism may be easily overlooked and the fluid reported as sterile Further the presence of some well known cause for suppurative meningitis such as ear disease staphylococcal infection etc suggests the diagnosis

Acute otitis media may give rise to symptoms closely resembling those of meningitis such as headache pyrexia vomiting head retraction and delirium In such cases examination of the ear which should be made a routine in all cases where meningitis is suspected will reveal tympanic distension the relief of which is followed by a speedy disappearance of the symptoms In this connection it must be borne in mind that meningitis and intracranial abscess seldom follow directly upon acute otitis but are usually the sequelæ of chronic otitis which has resulted in caries of the temporal bone When evidences of caries of the middle ear are present in a case presenting cerebral symptoms distinction has to be made between meningitis and abscess of the brain Here the presence of localising symptoms either temporal or cerebellar and the presence of papillœdema and any tendency to a temporary abatement of the symptoms point to the existence of an abscess and further lumbar puncture will in all but the rarest cases settle the point In cases of abscess in which cells and organisms are found in the cerebrospinal fluid these exist in small numbers only as compared with the copious cells and organisms present in the fluid of suppurative meningitis (see p 1409)

Treatment —In cases of meningitis secondary to mastoid disease the source of infection should be at once cleared out by surgical procedure As in the case of pneumococcal meningitis the prognosis and treatment of all forms of pyogenic meningitis have been profoundly altered by the introduction of sulphanilamide and its derivatives and of antibiotics and the treatment in general is the same as that which has already been described in the case of pneumococcal meningitis Meningitis due to *H influenzæ Ps pyocyanea* and to some strains of coliform bacilli has been shown to respond favourably to treatment with streptomycin and other antibiotics (see pp 10 and 13)

(4) TUBERCULOUS MENINGITIS

This disease results from the general invasion of the cerebro spinal leptomeninges by the tubercle bacillus and this organism invariably arrives in the meninges by the blood stream from some previously existing focus of tuberculous infection elsewhere and most commonly from caseous tracheo bronchial and mesenteric glands and tuberculous bone disease Occurring at all ages it is the form by far the most frequently met with in the second and third years of life

Ætiology —Tuberculous meningitis is rare during the first year of life and especially during the first 6 months Its greatest incidence is during the second and third years It is common throughout childhood and early adult life, after which it becomes increasingly rare though cases may be met with even in the elderly The sexes are equally affected The primary focus from which the organisms are carried to the meninges is most often a tuberculous bronchial or mesenteric lymph gland In consequence the most potent causes of the disease are exposure of the young child to cases of open tuberculosis and the drinking of infected milk

Sometimes the source of infection is tuberculous disease of the lungs of the uro genital tract of the abdomen of the ear of the joints or of bone Operations upon the sites of tuberculous disease may directly cause the dissemination of the tubercle bacilli and especially surgical procedures upon tuberculous intracranial tumours upon spinal caries and upon tuberculous disease of bones and joints The acute specific fevers and especially measles are sometimes the exciting causes of the disease Injury to the head sometimes determines the attack

Pathology —The essential change in tuberculous meningitis is the presence of an inflammatory exudate studded with discrete miliary tubercles in the pia arachnoid membranes particularly in the interpeduncular space and over the base of the brain

On removing the skull cap the dura is found to be so tense that it can only with difficulty be indented by the pressure of a finger When the dura is incised the cerebral convolutions are seen to be flattened and pressed firmly against the inner

surface of the dura No cerebrospinal fluid escapes from over the surface of the hemispheres In extracting the brain from the skull it is commonly ruptured and fluid escapes with a gush from the dilated ventricular system allowing the hemispheres to collapse The base of the brain especially the interpeduncular space is seen to be covered with a gelatinous greenish yellow exudate which surrounds the optic chiasma the emerging cranial nerves and infundibulum and the vessels of the circle of Willis and spreads out to the tips of the temporal lobes and to the stems of the Sylvian fissures Only rarely does this exudate spread on to the convex surfaces of the brain In cases of relatively long duration the exudate acquires a greyish colour and is tough in consistency and firmly adherent to the brain Close inspection of this inflammatory exudate shows it to be studded with innumerable small grey tubercles These are particularly numerous in relation to the blood vessels and they can be seen in large numbers along the course of the middle and anterior cerebral arteries The whole ventricular system is uniformly and greatly dilated and flakes of green gelatinous lymph may be found mixed with the cerebrospinal fluid contained in the distended ventricles Frequently small tubercles can be seen scattered over the walls of the ventricles and over the surface of the choroid plexuses Not infrequently discrete tuberculous foci may be found scattered through the substance of the hemispheres cerebellum and brain stem These vary in size from the pin point tubercles characteristic of the basal meninges to caseating masses the size of a marble Rarely thrombosis may be seen in one or other of the venous sinuses and occasionally areas of softening are found in the brain substances

The meninges of the spinal cord are usually also involved and tubercles may be seen upon the surface of the cord or the inner aspect of the dura mater

Examination of the rest of the body almost invariably shows the changes of general ised miliary tuberculosis the exception being those rare cases in which tuberculous meningitis has resulted from a tuberculoma in the substance of the brain

Symptoms —The onset is usually gradual with signs of vague and slight illness In children general apathy and neglect of amusements and play headache loss of appetite obstinate constipation dullness fretfulness restlessness at night with grind ing of the teeth during sleep headache vomiting and pyrexia are common symptoms In older subjects lassitude depression mental alteration perversity and hysterical manifestations are frequent Constipation is usually present and the breath has a peculiar fetor The facial expression is one of illness and frowning discomfort and there is disinclination to talk Young children may be speechless for days together As a rule in this stage of the disease young children complain of nothing and delirium is rare but as age advances delirium increases in frequency and headache usually frontal is increasingly complained of These slight and vague symptoms may last from a few days to several weeks and constitute what has been called the prodromal stage of the malady An early disappearance of the knee and ankle jerks and the occurrence of retention of urine are often early signs and should be looked for in suspected cases In those cases which are said to begin acutely careful enquiry will generally reveal that some symptoms such as the above have preceded the acute onset The further development of the disease is marked by the appearance of a lethargy which soon deepens into a stupor from which it is difficult or impossible to arouse the patient Vomiting is of frequent occurrence and headache may be severe The child lies upon its side in a cramped position resenting any disturbance The expression becomes vacant with wide open eyes and dilated pupils as if the gaze were fixed upon some distant object There is often some retraction of the angles of the mouth and there is frequently a bright malar flush In the later stages the limbs are generally extended and rigid Stiffness of the neck is the rule and head retraction may occur but this is never so marked as in pyogenic meningitis The abdomen is always markedly retracted and a tache cerebrale is often conspicuous A single sharp cry apparently causeless called the hydrocephalic cry which is common in all

forms of meningitis and also in other infantile intracranial affections is sometimes heard

Ocular phenomena make their appearance towards the end of the first week of the developed disease All varieties of varying and persistent strabismus and ptosis are met with paralysis of the external rectus being the most common Rolling movements and independent movements of the eyeballs may occur None of these signs is constantly present The pupils may be contracted at first and may show varying inequality but in the later stages they are dilated Papilloedema is often present *towards the end of the second week if the patient survives so long It is of moderate* intensity the height of the swelling rarely exceeding two dioptres Choroidal tubercles sometimes occur

Convulsions are common in every stage of the disease in children but rare in adult cases They may be the first symptom of the onset but are more often met with in the later stages of the disease They may be local or general Repeated rhythmic movements are frequent and are specially noticeable in connection with the mouth where sucking and champing movements and grinding of the teeth are common Rhythmic movements of the limbs may also occur Coarse tremor upon movement of the limbs is the rule, and spasmodic twitching of the muscles is frequent In rare cases, movements exactly like those of chorea occur Kernig s sign is usually present

The temperature is usually raised one or two degrees but it presents no characteristic features Irregularity of the pulse is the rule and is of considerable diagnostic importance Rapid in the early stages it tends to become unduly slow in the stage of coma and again rapid as death nears Cheyne Stokes breathing and grouped breathing are common Constipation is usually a marked and persistent feature

Diagnosis—The early symptoms of the disease may give rise to difficulty in diagnosis but this is relatively simple when the disease is advanced The diseases liable to be confused with tuberculous meningitis at its commencement are other forms of meningitis virus diseases of the nervous system especially acute poliomyelitis cerebral abscess the exanthemata—especially enteric fever—and pneumonia It must be borne in mind that in children convulsion strabismus head retraction and stiffness of the neck with pyrexia may be symptomatic of many maladies apart from meningitis especially of apical pneumonia When signs of meningeal irritation are unmistakable the condition has to be distinguished from the various forms of pyogenic meningitis In the latter the degree of meningism is usually more intense and the cerebrospinal fluid reveals a turbid or purulent fluid with a predominantly polymorph pleocytosis and the causative organism can usually be cultured

Poliomyelitis and other virus infections of the nervous system can at their commencement closely simulate tuberculous meningitis and it is in such cases that the retention of the cerebrospinal fluid chlorides and glucose at their normal level can be such a valuable aid to diagnosis

The meningeal reaction apt to arise from time to time in cases of cerebral abscess may closely resemble tuberculous meningitis and may be associated with a mixed pleocytosis and a sterile fluid

In any case suspected of being one of tuberculous meningitis a diagnostic lumbar puncture should be carried out without delay as the success of modern treatment is much influenced by the time of its commencement The characteristic features of the fluid are that it is usually under considerable pressure it is clear or only slightly turbid, has no visible deposit before centrifugalisation but it often forms a fine flocculent clot It contains an excess of albumin The normal sugar is reduced or absent and a value over 50 mg per 100 ml practically excludes the diagnosis It is sometimes between 40 and 50 mg per 100 ml but in the majority values under 30 mg are obtained In other forms of non purulent meningitis such a poliomyelitis and benign *lymphocytic meningitis the glucose content of the cerebrospinal fluid is*

almost invariably normal Early reduction of the chloride content below 700 or even 650 mg per cent is of value in distinguishing tuberculous meningitis especially from virus diseases of the nervous system There is a pleocytosis with a high proportion of lymphocytes 70 to 80 per cent being of this nature and the rest being polymorphonuclears Careful examination will reveal the presence of the tubercle bacillus in more than half the cases and their presence can be readily demonstrated by injecting the fluid into the subcutaneous tissue of guinea pigs when the characteristic lesion of tubercle results and also by culture It must be remembered that in some cases the polymorphonuclear leucocytes may be in excess but these cases are at once distinguished from other forms of meningitis by the presence of numerous lymphocytes by the absence of the meningococcus and of the other pyogenic organisms and by the presence of the tubercle bacillus

Course and Treatment —Before the advent of streptomycin tuberculous meningitis was invariably fatal and usually ended in the patient s death in from 3 to 8 weeks of the onset of symptoms

To day provided that early diagnosis is achieved the vigorous use of streptomycin together with sodium aminosalicylate (P A S) and isoniazid (I N H) should result in recovery in at least 50 per cent of cases

Streptomycin is administered both intrathecally and intramuscularly and either sodium aminosalicylate or isoniazid by mouth continuously for the initial period of 8 to 12 weeks If general improvement as measured by appetite weight subsidence of fever and loss of drowsiness is satisfactory and is confirmed by a gradual return of the cerebrospinal fluid towards normal a rest of 1 month in intrathecal treatment alone should be given At the end of this period a further course should be given and thereafter a gradual withdrawal of treatment may be achieved provided always that improvement is maintained Good results are now being obtained using isoniazid (*e g* 100 mg t d s) combined with streptomycin administered only by the intra muscular route (*e g* 1 g daily) thereby avoiding the need for daily intrathecal injections The addition of cortisone to this regime is still *sub judice*

Careful observation at increasing intervals must be maintained over a period of 5 years

Prominent among the complications which may arise are chronic hydrocephalus from the development of a plastic meningeal fibrosis around the base of the brain and leading in its turn to double hemiplegia convulsions blindness and imbecility and deafness from the degeneration in the cochlear nerves resulting from the use of intra thecal streptomycin

(5) BENIGN LYMPHOCYTIC MENINGITIS (CHORIO MENINGITIS)

Synonyms —Epidemic Serous Meningitis Benign Aseptic Meningitis

Ætiology —The causative agent is unknown but there is evidence that one or more neurotropic viruses are responsible No organisms have been found in the cerebro spinal fluid The disease has been transmitted to animals by injection of cerebro spinal fluid obtained in the acute stage of the affection The malady so named appears to be of wide distribution

Pathology —Since recovery is the rule nothing much is known of this but lymphocytic infiltration of the lepto meninges has been found in one fatal case

Symptoms —Children are mostly affected but no age appears exempt The onset is abrupt with headache sickness and fever The typical signs of meningeal irritation are present neck and spine rigidity Kernig s sign irritability and restlessness and sometimes delirium Somnolence is unusual In young children convulsions may occur The fever mounts to 102 or 103 F and fluctuates It may disappear in 2 or 3 days or persist for 3 weeks Lumbar puncture yields a cerebrospinal fluid under pressure usually clear but sometimes opalescent The cell count ranges from

50 to 1500 per c mm After the first 2 or 3 days these cells are almost wholly lymphocytes The sugar and chloride contents remain at normal height thus differing from the findings in other forms of acute lepto meningitis, and resembling the findings in acute poliomyelitis

Diagnosis —This depends upon the cerebrospinal fluid findings and upon the benign course of the illness For a few days differentiation from poliomyelitis may be impossible

Prognosis —Recovery is the rule

Treatment —Repeated lumbar puncture reduces the intracranial tension Beyond this only general nursing care is needed

(6) SYPHILITIC MENINGITIS

Meningitis due to infection by *Treponema pallidum* is one of the characteristic lesions met with in practically all cases of syphilitic disease of the central nervous system and plays its part in the production of the symptom complexes of these maladies from acute cerebral syphilis and acute myelitis to general paralysis and locomotor ataxy It may occur at any period after infection, but one half of the cases occur during the first 4 years In a few cases the symptoms have been noticed co incidently with the syphilitic roseola

Pathology —The morbid process consists essentially in an infiltration of the meninges with lymphocytes and plasma cells spreading from the perivascular spaces where the spirochætes multiply freely, and it may lead to scarring and opacity of the membranes with consequent strangling of the nerves and vessels and occlusion of the arachnoid space or to massive gummatous formation in the meninges It is essentially a chronic form of meningitis though it may result in the production of acute symptoms A marked feature is that the meningeal changes may be found actively progressive in one spot and equally regressive in another The disease may be local or diffuse and it may attack the dura (pachymeningitis) and involve the over lying bone or it may spread from the pia arachnoid into the sublying nervous tissue (meningo encephalitis)

The cerebrospinal fluid is characteristic It is usually under increased pressure is clear and colourless and contains lymphocytes and no other cell forms The number of the lymphocytes present is in direct proportion to the activity of the meningeal syphilis The spirochæte has rarely been found in the fluid yet inoculation of apes with the fluid has proved successful

Symptoms —Apart from those conditions of nervous syphilis in which meningitis is associated with arterial disease the formation of massive gummata and neuronic degeneration syphilitic meningitis may be described as giving rise clinically to the following conditions

1 *Headache*

2 *Hydrocephalus* —In those acute cases of cerebral syphilis characterised by rapidly oncoming headache, vomiting and papillœdema mental reduction and somnol ence without localising symptoms and which respond readily to treatment, it seems certain that ventricular distension, consequent upon adhesive meningitis and ependy mitis is responsible A more slowly oncoming ventricular occlusion may give rise to symptoms which cannot be distinguished from those caused by a non localisable intracranial tumour Syphilitic meningeal occlusion may give rise to typical hydro cephalus and a considerable proportion of the cases of infantile hydrocephalus are of this nature and are due to congenital syphilis A few cases are recorded in which chronic hydrocephalus of this nature has occurred in adult life

3 *Infantile syphilitic meningitis* —This is a chronic malady which commences insidiously during the first few months of life with signs of general nervous deteriora tion The appearance of the brain is very characteristic The membrane over the

vertex is opaque and thickened and adherent to the cortex The gyri are shrunken the sulci wide and the surface of the brain has in parts the appearance of wash leather The child does not get on and takes an ever decreasing notice of its surroundings Power of movement lessens the limbs become rigid and the clinical aspect comes to resemble exactly that of a severe cerebral diplegia Convulsions are of frequent occurrence The diagnosis is not difficult for the signs of meningitis are obvious and those of congenital syphilis may be present There is an excess of lymphocytes in the cerebrospinal fluid both in which and in the blood there is a positive Wassermann reaction The prognosis in any case where the symptoms have become marked is most unfavourable

4 *Adult syphilitic meningitis* with a symptom complex closely resembling that of tuberculous meningitis has been reported on many occasions (see pp 1395 1461)

5 *Paralysis of cranial nerves*—This common and often isolated symptom of nervous syphilis may result from sclerosing basal meningitis or from the presence of a gumma in the course of the nerve Several of the nerves may be involved together in one patch of meningitis Any of the cranial nerves may be affected from the olfactory to the hypoglossal but the third or oculo motor nerve is by far the most frequently attacked

Treatment—The treatment of the above conditions is that appropriate for nervous syphilis in general (pp 223 1461) Penicillin is now the treatment of choice but a diminishing number of physicians still prefer to follow it up with courses of bismuth and organic arsenic by injection Iodide of potassium is also of value and should be administered over a long period

MENINGISM

The term meningism is used for a group of cases which present symptoms of meningitis and in which no pathological change can be found either in the cerebro spinal fluid or if death occur in the meninges or cerebral tissue It is met with in children in association with acute febrile diseases and is presumably due to the toxin present Recovery is usually rapid and complete

HYDROCEPHALUS

Definition—The term hydrocephalus denotes an abnormal accumulation of cerebrospinal fluid within the skull This may be confined to the ventricular cavities giving rise to the variety known as internal hydrocephalus or it may involve both the ventricular and the general subarachnoid spaces a condition referred to as communicating hydrocephalus This distension is associated in many cases with an expansion of the cranial bones and enlargement of the skull

General Considerations—Theoretically this abnormal increase of fluid may result from one or more of three causes viz (1) excessive production of fluid (2) interference in the normal flow of fluid and (3) defective absorption The fluid is normally produced by the choroid plexuses of the ventricles and flows through the ventricular system into the general subarachnoid space by way of the foramina of Luschka and Magendie in the roof of the fourth ventricle It then fills the basal cisterns and passing forward between the tentorium cerebelli and the brain stem flows up over the cerebral hemispheres to be absorbed by the arachnoid villi which project into the walls of the venous sinuses and discharge their contents into the venous blood stream Some of the fluid passes downwards into the spinal subarachnoid space but it is estimated that only one tenth of the fluid is absorbed from arachnoid villi in the spinal spaces

Of the causes of hydrocephalus the most important and the one of which we have the most precise knowledge is obstruction of the normal cerebrospinal flow and it

is evident that this obstruction may occur at several different points and be produced by a great variety of pathological causes Some of these are known and some remain obscure It will thus be seen that hydrocephalus is the end result of a variety of causes and until our knowledge is more complete it is most satisfactorily classified on a clinical basis and described as a number of clinical pictures which recur with some frequency

The following principal varieties of hydrocephalus are met with (1) congenital hydrocephalus, (2) chronic acquired hydrocephalus and (3) acute acquired hydrocephalus

In the majority of cases in which general atrophy of the cerebral tissues occurs fluid accumulates both in the ventricles and in the subarachnoid space but such compensating enlargement is not to be regarded as in any sense of the same nature as true hydrocephalus Such accumulation of fluid is found in cases of cerebral diplegia general paralysis of the insane cerebral arteriosclerosis and chronic alcoholism and it also occurs in the brains of old people It is merely the result of wasting and shrinkage of the brain tissue and the accumulation of fluid takes place in order to fill the space within the rigid skull which is thus vacated

(1) CONGENITAL HYDROCEPHALUS

Ætiology—Hereditary influences are of importance in the causation of congenital hydrocephalus This disease frequently affects several children of the same parents and it may even appear as a striking familial disease affecting members of several generations of the same stock Spina bifida meningocele and hydromyelia are of frequent occurrence in association with this condition and irregular or arrested development of the brain stem and cerebellum particularly the Arnaldo Chiari malformation are common Among other bodily abnormalities not infrequently associated with the affection may be mentioned hare lip cleft palate talipes rectal and testicular ectopia and imperforate anus In a few cases definite syphilitic lesions of the ependyma of the brain stem in the region of the aqueduct or fourth ventricle have been found In many cases the ætiology remains completely unknown

Pathology—The quantity of fluid which is found in the ventricles after death varies greatly usually being 15 to 20 oz In long standing cases with great cranial enlargement very large quantities have been met with The character of the fluid does not usually greatly differ from that of normal cerebrospinal fluid Its specific gravity varies from 1 008 to 1 010 It is clear and colourless or occasionally slightly yellow It contains a very small quantity of albumin and a normal quantity of chlorides The dilatation of the lateral ventricles is more extensive than that of the third and fourth ventricles and is usually symmetrical upon the two sides *It affects the* body more than the cornua of the ventricles so that the central cortex is most thinned The foramina of Monro are greatly enlarged and the anterior pillars wasted The convolutions are flattened and the sulci indistinct The thickness of the cerebral substance is much reduced In advanced cases the cerebral hemispheres have the appearance of thin walled sacs which collapse entirely when the contained fluid is allowed to escape In a few cases the aqueduct has been found closed as if by an antecedent ependymitis

Symptoms—In congenital hydrocephalus the enlargement of the head is the first noticeable feature It may take place during intra uterine life and it may be so great as to make delivery impossible without destruction of the head More frequently the cranial enlargement not noted at the time of birth becomes evident during the first weeks of life The increase usually affects all the diameters of the cranial cavity and is most marked at the vertex and least at the base Trousseau compared the opening out of the cranial bones, which occurs as the head enlarges to the falling back of the petals of an opening flower The forehead is large rounded,

and projects forward the temporal fossæ are obliterated and the parietal eminences carried backwards The vertex is often somewhat flattened as also may be the occipital region The direction of the external auditory meatus alters with the increasing size of the head normally directed obliquely forwards it comes to look directly inwards or even obliquely backwards in severe cases The head is frequently asymmetrical The sutures may be widely open and then there is marked bulging along these lines and at the fontanelles The skull may attain enormous dimensions, and it may be beyond the child s power to lift or even move the head Many examples are recorded in which the circumference has been from 60 to 80 cm The face is characteristically triangular contrasting markedly with the forehead Wasting of the facial subcutaneous tissues and retarded development of the maxilla and mandible often render the contrast still more striking Bulging of the orbital plates of the frontal bones presses down the eyeballs so that the pupils become more or less covered by the lower lids and a band of the sclerotic may be visible between the iris and the upper lid The hydrocephalic child often uses his hands to depress the cheeks and so draws down the lower lids out of the position which they impair the line of vision The hair of the head becomes scanty the subcutaneous veins of the scalp are often greatly developed and distended ands ometimes a vortex of dis tended veins radiates from the region of the anterior fontanelle Percussion of the skull gives a characteristic hollow cracked pot note

The general nutrition is poor and bodily development retarded in proportion to the severity of the effect of the hydrocephalus upon the nervous system The nervous symptoms which appear during the course of congenital hydrocephalus are both variable and inconstant depending upon the severity of the condition and the rate at which it progresses They may be summed up in the following list in order of frequency convulsions mental failure spastic paralysis of the limbs optic atrophy deafness nystagmus headache papillœdema and vomiting There is no constancy regarding these symptoms Convulsions may be absent and mental acuity may be unimpaired Spastic weakness occurs in less than half the cases optic atrophy still more rarely and papillœdema is distinctly unusual

Convulsion —While it is to be borne in mind that the whole course of hydro cephalus in children may run without the occurrence of convulsion yet in the majority of cases this symptom is conspicuous In some of the post natal cases the symptoms of cerebral disorder are ushered in by convulsion and it is probable that in many cases such convulsions are the immediate expressions of the morbid process of which the primary hydrocephalus is the final result The convulsions which recur at intervals throughout the course of the majority of cases of hydrocephalus result from a condi tion of functional instability of the cerebral cortex which long continued increased intracranial pressure brings about The convulsions are usually general with loss of consciousness

Mental impairment —All degrees of mental reduction occur from the least notice able to complete idiocy The more severe forms are met with in cases when cerebral agenesia and porencephaly are associated The psychical reduction is less prominent the greater the age at which the symptoms commence and as a rule the intelligence is far greater than the severity of symptoms (cranial enlargement paresis etc) might lead one to expect Cerebration is usually slow and the disposition placid and periods of somnolence are of common occurrence

Paralysis —The effect of long continued ventricular distension in many cases is to cause degeneration of the pyramidal system and according to its degree the latter entails bilateral spastic paralysis with contracture The first signs of the onset of this event are exaggeration of the deep reflexes and the change in type of the plantar reflexes from the flexor to the extensor response The lower extremities are affected earlier and to a greater extent than are the upper and at one period of the disease a case may present the picture of cerebral diplegic rigidity comparable with that of

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Little's disease The upper extremities are affected later The paresis of the limbs is almost always symmetrical and equal upon the two sides Sensibility is generally normal

Vision is interfered with in a considerable proportion of the cases The enlargement of the infundibular portion of the third ventricle by pressure upon the inner borders of the converging optic tracts may cause bitemporal hemianopia with atrophy of the nasal portions of both optic discs this condition subsequently progressing to complete blindness and complete optic atrophy

In rare cases optic atrophy is the result of papillœdema Strabismus is commonly present and it is most frequently convergent Nystagmus is met with in the subjects of hydrocephalus who are blind from optic atrophy and it is of frequent occurrence in *long standing cases in which spastic paresis is well marked*

Headache is rarely complained of and never dominates the clinical picture in children and is never so severe and persistent as that arising from the presence of an intracranial growth Cerebral vomiting is of comparatively rare occurrence

When one considers the *profound anatomical alterations which take place in the* advanced stages of the disease the occurrence in some cases of unusual symptoms indicative of interference with the functions of the cerebellum brain stem and cranial nerves is easily explicable Unilateral or bilateral ataxy vertigo deafness, anosmia and paralysis of cranial nerves are the most important of such unusual symptoms

The signs of failure of the nervous system as a whole usher in the fatal result in severe cases For some days or perhaps weeks before death hebetude may become profound spastic paresis gives place to flaccid paralysis with muscular wasting the deep reflexes disappear and the sphincter mechanism loses its control and subsequently its tone

Diagnosis —On account of the characteristic appearances of the skull this seldom presents any difficulty though in childhood only a careful history will serve to differentiate the congenital from the chronic acquired type of hydrocephalus The enlarged skull of rickets is recognised by its different conformation by the absence of nervous signs with the possible exception of convulsions by the absence of the characteristic change in the percussion note and by the presence of other rachitic signs The rare condition of macrocephaly is not associated with any distortion of the relative proportions of the skull *It should be remembered that an abnormally large head is* hereditary in some families

Prognosis —In all severe and progressive cases the prognosis is hopeless In some of the milder cases the process becomes arrested and the patient may attain to adult life with the possession of all his faculties In cases in which the disease becomes stationary the prognosis as regards mental capacity and the continuance of recurring convulsions has to be considered If the mental capacity at the time of the arrest is fair it is not likely to deteriorate further unless epilepsy is established When mental reduction is marked at the time of arrest any appreciable degree of improvement cannot reasonably be expected *A certain number of cases of mild* congenital hydrocephalus cease to progress and the symptoms retrogress and disappear permanently

Treatment —In those cases in which there is evidence of congenital syphilis *the employment of antisyphilitic treatment is indicated*

The results of surgical interference for the relief of pressure or to attempt the re establishment of a way of escape for the cerebrospinal fluid have been, up to the present so unsatisfactory that many writers and authorities consider such measures unjustifiable It should be remembered however that in severe and progressive cases one is dealing with a necessarily fatal malady and a few encouraging results have been published which appear to justify further investigation Ventricular paracentesis is useless as any relief which results is only temporary and it is not without danger if the intraventricular pressure is raised

(2) CHRONIC ACQUIRED HYDROCEPHALUS

Ætiology —Hydrocephalus usually of the internal type secondary to obstruction in the cerebrospinal fluid pathway may result from a variety of causes Foremost among these is meningitis especially the posterior basic meningitis of infancy and early childhood but it may result from any type of meningitis including tuberculous meningitis in which recovery from the initial disease takes place It is caused by occlusion of the foramina of Luschka and Magendie and results in a uniform dis tension of the entire ventricular system Another group of cases depends upon a primary non neoplastic stenosis of the aqueduct of Sylvius as described by Stookey and others Some of these cases show a proliferation of the sub ependymal glia with constriction of the lumen of the aqueduct In others the ependyma may undergo proliferation with the development of tufts which project into the lumen of the canal and form valve like obstructions to the flow of fluid Again in others the lumen itself may be split up into a number of minute channels hardly visible to the naked eye The ultimate cause of this aqueductal atresia is unknown In a third group acquired hydrocephalus results from the presence of neoplasms of slow growth which obstruct the cerebrospinal fluid channels of these the slowly growing cerebellar astrocytomas of early childhood are the most important Other causes are cysts and slowly growing tumours of the third and fourth ventricles supra sellar (Rathke pouch) cysts and pineal or other tumours of the mid brain

Symptoms —The symptoms of chronic acquired hydrocephalus depend largely upon the age at which the process starts If the malady begins in early infancy the picture is in all respects similar to that of congenital hydrocephalus If it occurs in early childhood before the sutures of the skull have become fused and the bones of the vault indistensible the picture is that of moderate hydrocephalus combined with the symptoms and signs of raised intracranial pressure

Pressure symptoms often begin abruptly after the signs of hydrocephalus have been present for a considerable time Prominent among these are headache usually paroxysmal in character vomiting strabismus and double vision In such cases papillœdema is common and if left unrelieved leads to failure of vision from consecutive optic atrophy which may come on with very great rapidity In long standing cases mental failure may occur and weakness and inco ordination of movement from a combination of disturbances of the pyramidal and cerebellar systems There may be considerable arrest of physical development and in cases extending into later childhood puberty is commonly delayed or complete infantilism may persist

Treatment —In some cases of acquired hydrocephalus the cause can be removed by surgical operation and cure may result To this category belong those due to tumour or cyst formation Various methods of re-establishing the cerebrospinal fluid flow have been devised in cases of stenosis of the aqueduct or occlusion of the meningeal foramina The most successful of these is Torkildsen s operation in which the aqueduct is by passed by means of a plastic or rubber catheter introduced into the posterior horn of one of the lateral ventricles and passing under the scalp to enter the spinal subarachnoid space through the antlanto occipital membrane As in congenital hydrocephalus the different forms of ventriculostomy have proved dis appointing and external decompressions usually only afford temporary relief quickly followed by the added complications of cerebral herniation

(3) ACUTE ACQUIRED HYDROCEPHALUS

This condition results from rapid and severe obstruction to the flow of cerebrospinal fluid in subjects whose skulls are no longer capable of expansion or in the case of children when the expansion of the skull cannot keep pace with the ventricular distension Therefore unlike the congenital and the chronic forms of hydrocephalus

there is little or no enlargement of the head and the clinical picture is that of raised intracranial pressure usually without localising signs

Ætiology —In former times the term acute hydrocephalus was applied to tuberculous meningitis and ventricular distension indeed plays an important part in the evolution of this malady The use of the term in this connection has however fallen into disuse The common cause of the condition is new formation within the skull in such a position as to obstruct the flow of cerebrospinal fluid It is thus most often met with in tumours of the third and fourth ventricles and of the posterior cranial fossa

Symptoms —These are the general symptoms of increased intracranial pressure of rapid onset and great severity The majority of cases present themselves with the symptom complex of headache, vomiting and papillœdema without signs of any local lesion of the hemispheres or cerebellum In severe cases proptosis may be present distension of the veins of the scalp may be seen and the skull commonly has a characteristic cracked pot' percussion note Radiological examination may reveal a mottled appearance of the vault resembling that of beaten silver and there may be some decalcification of the posterior clinoid processes and general flattening of the cavity of the sella turcica The diagnosis is confirmed by ventriculography

Treatment —This is essentially that of the underlying cause

(4) OTITIC HYDROCEPHALUS

This term has been used to describe certain cases of raised intracranial pressure occurring in the course of middle ear suppuration which appear to be due to an abnormal accumulation of cerebrospinal fluid

The condition usually occurs in children and has to be distinguished from cerebral abscess Headache vomiting papillœdema and squint are common but unlike cases of abscess there is little if any toxæmia and the cerebrospinal fluid remains normal except for an increase in its pressure

There is evidence that the condition is caused by a non suppurative thrombosis of the cortical veins or venous sinuses and similar cases have been described as a complication of other localised infective processes *e g* tonsillar infections (see p 1410)

The illness runs a benign course and complete recovery normally ensues The intracranial hypertension may be controlled by repeated lumbar puncture

ENCEPHALITIS

Inflammation of the brain may be met with under widely different clinical associations It may occur as a primary disease or as a complication of known infective processes affecting the system locally or generally and it may occur as an associated event in diseases of the meninges As a primary condition it is met with in a variety of virus diseases of the nervous system pre eminent amongst which is encephalitis lethargica These are described in a later section It is found as the result of infection of the brain with pyogenic organisms derived either from local sources of infection in the neighbourhood of the brain or from pyæmia and it may then be either suppurative (brain abscess) or non suppurative It may occur as a complication of many of the acute specific fevers especially measles vaccinia and mumps In these the encephalitis may only be a part of a general inflammation of the nervous system—an encephalo myelitis Acute encephalitis may be found in rare cases as the sole manifestation of cerebral syphilis

In all forms of meningitis there is some degree of extension of the inflammation into the brain tissue and this assumes an important degree in tuberculous meningitis and in some cases of epidemic cerebrospinal meningitis

The symptoms common to all forms of encephalitis are the general symptoms of severe intracranial disease—headache somnolence coma irritability delirium convulsions and vomiting and, in addition local symptoms of irritation and paralysis the precise nature of which is determined by the position and extent of the lesions

(1) CEREBRAL ABSCESS

Synonym —Suppurative Encephalitis

Ætiology —Suppuration within the brain is never primary but is the result of extension of infection from neighbouring tissues or through the blood stream from foci of infection in distant organs In rare cases the original focus of infection is undiscoverable

The following are the important causal factors

1 *Direct infection* from infected regions in the immediate vicinity (*adjacent abscess*) —The important cause of infection is any form of infective disease in the bones or soft tissues of the head and neck From 60 to 70 per cent of all cerebral abscesses arise in this way By far the most common cause is chronic suppuration in the middle ear and petrous temporal bone particularly when this is complicated by a superimposed acute infection Infection of the frontal or other accessory nasal sinuses is second only in importance to middle ear disease and chronic infections of the bones of the skull suppuration of the scalp orbital cellulitis carbuncles of the neck and face are other causes

Adjacent abscesses are usually solitary and commonly occur in the part of the brain in closest proximity to the primary focus of disease Thus abscesses secondary to ear disease are usually situated in the corresponding temporal lobe or cerebellar hemisphere those resulting from disease of the nasal sinuses in the frontal lobes and so one Exceptions to this generalisation are however met with

The exact manner in which the infection spreads to the brain probably varies in different cases In some it occurs by a septic thrombosis of a vein communicating between the infected region and the underlying brain In others the organisms gain access to the brain substance by spreading along the perivascular spaces from a localised area of meningitis evoked by the primary disease In others still there may be direct spread by continuity through the process of ulceration of the surface of the brain described by MacEwen When the primary disease affects the upper surface of the petrous bone the abscess is commonly situated in the temporal lobe which may be adherent to the tegmen tympani while if the posterior surface of the petrous bone is affected the abscess is usually in the cerebellum In cases both of direct extension and spread through the perivascular spaces the cerebrospinal fluid shows the presence of leucocytes predominantly polymorphonuclear during the stage of invasion indicating that the meninges have been involved even though no symptoms of meningitis are present The organisms responsible are commonly streptococcus pneumococcus or staphylococcus The infection may be mixed Other pyogenic organisms may be found and rare cases are caused by streptothrix infection

2 *Pyæmic states* —Abscesses resulting from infection through the blood stream are termed *metastatic or hæmatogenous abscesses* and comprise from 20 to 25 per cent of the total They commonly arise as a complication of chronic suppuration in the chest such as bronchiectasis empyema or lung abscess Less commonly they occur as a complication of chronic bone disease puerperal septicæmia acute infective endocarditis or other septicæmic conditions Subacute bacterial endocarditis may lead to multiple embolic foci of encephalitis but not to actual abscess formation Rarely metastatic abscesses may arise from localised suppuration in remote parts such as the liver and appendix where there has been no evidence of a pyæmic state It is probable that the 10 per cent of cases of cerebral abscess in which no primary

cause can be found fall into this category the original focus of disease having undergone complete resolution

Metastatic abscesses are commonly multiple but may be solitary They are usually situated in the cerebral hemispheres and originate at the junction of the cortex and subcortical white matter or in the central grey masses They are rare in the cerebellum and brain stem The organisms responsible are streptococcus staphylococcus and pneumococcus and mixed infections may occur

3 *Trauma*—Traumatic abscesses may result from penetrating wounds of the skull, particularly when fragments of metal clothing bone and scalp are carried into the brain Such cases are extremely rare in peace but assume considerable importance in times of war Fracture of the base of the skull may permit infection to gain access to the brain from the middle ear or naso pharynx Fractures involving the inner wall of the frontal sinuses or cribriform plate may be followed by the development of a cerebral abscess after a long latent interval

Pathology—Cerebral abscess—whether adjacent or metastatic in origin—usually commences at the junction of the cortex and the subcortical white matter As it increases in size the surrounding brain tissue is displaced and severe distortion of the brain and ventricular system results The commonest site is the temporal lobe and approximately half of all cerebral abscesses are found in this region a reflection of the importance of middle ear disease as an ætiological factor The frontal lobes and the lateral lobes of the cerebellum are other areas frequently affected Abscess in the parietal or occipital lobes or brain stem is rare

If it has been left unmolested until the patient s death a cerebral abscess may attain the size of a hen s egg or even of a large orange but many lead to a fatal outcome before they attain such dimensions The cavity contains thick greenish yellow pus which is often extremely fetid Commonly the abscess cavity is multilocular and its interior is usually of a greyish green colour and covered with adherent purulent debris The abscess wall varies greatly in character with the age of the abscess In cases of recent origin there may be only a slight line of demarcation between the ragged irregular cavity and the surrounding brain If the abscess has been present for a few weeks a well defined capsule can be seen and this can often be felt by the exploring cannula at operation In chronic cases the capsule may become so thick that the whole abscess can be shelled out of the brain without rupture The pus in such an abscess may become inspissated and sterile The white matter for a wide area surrounding an abscess is very œdematous and may contain areas of softening and fresh abscess formation The more acute the abscess the more marked is the surrounding œdema The surface of the brain overlying an abscess often shows a localised area of meningitis with flakes of purulent lymph adherent to the pia mater

The earliest stages of the development of a cerebral abscess seldom come under direct observation but there is every reason to suppose that the initial process is the development of an area of encephalitis around the nidus of invading organisms In this area there is a mobilisation of inflammatory cells with dilatation of capillaries and œdema Gradually liquefaction and pus formation take place in the centre while a fibroblastic reaction at the periphery gives rise to the abscess wall Outside this again is a neuroglial proliferation together with a diffuse inflammatory infiltration of the brain substance and perivascular spaces

Many cases of abscess are associated with a terminal spreading meningitis and in a proportion of cases rupture may have occurred either into the ventricles or the general subarachnoid space a complication which is invariably fatal within a few hours In adjacent abscesses it is not uncommon to find an associated subdural or extradural abscess which is invariably in direct contact with the primary focus of disease

Symptoms—A cerebral abscess has its origin in inflammation and constitutes when developed a foreign body within the skull Death may result from the effects

of continually increasing intracranial pressure and wide interference with cerebral function or from the spread of the infection from the abscess to the meninges and general subarachnoid space The symptoms may be grouped in four classes (1) Those of local suppuration (2) those of increased intracranial pressure (3) localising signs dependent upon the position of the abscess and (4) those of the terminal extension of the infective process

The onset of symptoms is usually extremely insidious and is apt to be overshadowed by those of the preceding disease The usual sequence of events is that a case of mastoid suppuration or frontal sinusitis does not progress quite as well as it should do as judged by the local condition and gradually the picture of cerebral abscess makes its appearance without it ever being possible to state with certainty where the original illness ended and the complication began Similarly with blood borne infections it is seldom possible to determine with precision the time at which an abscess began to form although occasionally a rigor may mark the time of onset

The earliest and most constant symptom is headache This is characteristically intermittent in the early stages felt across the forehead and in the occipital region irrespective of the site of the abscess especially on rising in the morning and accentuated by coughing sneezing or stooping The pain attains to an agonising degree of intensity and gradually becomes more prolonged frequent and severe until drowsiness begins to dim its severity In some cases a considerable degree of local pain and hyperæsthesia to touch or pressure may be felt over the site of an abscess Occasionally during the months in which a slowly developing abscess is forming there may be periods lasting a day or two of intense occipital pain nuchal rigidity vomiting and fever These disturbances may pass as bilious attacks or influenza but are in reality due to meningeal irritation set up by a deeply seated infection Vomiting is a common early symptom It usually occurs with the headaches but especially in cases of cerebellar abscess it may arise suddenly and with great violence in the absence of any other symptoms Mental changes are common These vary from slight lassitude and a vague feeling of unwellness to drowsiness and ultimately coma Delirium is common during periods of meningismus Double vision is often complained of and is usually an intermittent uncrossed diplopia on lateral deviation of the eyes which results from weakness of one or both external recti

Symptoms of focal disturbance of the nervous system are less constant and usually later in occurrence than the symptoms of general intracranial disorder Epileptic disturbances of any kind may occur with abscesses in the cerebral hemispheres taking the form of generalised convulsions focal fits or petit mal attacks according to the site of the lesion There may be weakness on one side of the body or in one limb or sensory disturbances of a similar distribution Disorders of vision due to the presence of hemianopia may be encountered and disturbances of speech are common in abscesses of the left temporal lobe Where the cerebellum is involved the patient may be aware of awkwardness of voluntary movement particularly with regard to standing and walking and giddiness may be complained of

The patient usually has a strikingly sallow earthy complexion with a slightly cyanotic tint about the lips and nose The tongue is thickly coated the breath extremely offensive the lips dry and cracked and often bleeding from being picked The temperature chart is usually characteristic Fever is present but of a very low degree seldom rising above 100 F and often being subnormal for a day or 2 days at a stretch When it rises above 101 F it will usually be found that this rise is coincident with symptoms of meningism In chronic cases the patient may appear to be completely afebrile but careful recording will usually demonstrate an occasional rise to 99 or 100 F sometimes at intervals of many days Equally valuable is a record of the pulse rate This is almost always unnaturally slow and in no intracranial condition with the possible exceptions of extradural and subdural hæmorrhage is this depression of the pulse rate so constant as in cerebral abscess In persons with a

cause can be found fall into this category the original focus of disease having undergone complete resolution

Metastatic abscesses are commonly multiple but may be solitary They are usually situated in the cerebral hemispheres and originate at the junction of the cortex and subcortical white matter or in the central grey masses They are rare in the cerebellum and brain stem The organisms responsible are streptococcus staphylococcus and pneumococcus and mixed infections may occur

3 *Trauma* —Traumatic abscesses may result from penetrating wounds of the skull particularly when *fragments of metal clothing bone and scalp are carried into* the brain Such cases are extremely rare in peace but assume considerable importance in times of war Fracture of the base of the skull may permit infection to gain access to the brain from the middle ear or naso pharynx Fractures involving the inner wall of the frontal sinuses or cribriform plate may be followed by the development of a cerebral abscess after a long latent interval

Pathology —Cerebral abscess—whether adjacent or metastatic in origin—usually commences at the junction of the cortex and the subcortical white matter As it increases in size the surrounding brain tissue is displaced and severe distortion of the brain and ventricular system results The commonest site is the temporal lobe and approximately half of all cerebral abscesses are found in this region a reflection of the importance of middle ear disease as an ætiological factor The frontal lobes and the lateral lobes of the cerebellum are other areas frequently affected Abscess in the parietal or occipital lobes or brain stem is rare

If it has been left unmolested until the patient s death a cerebral abscess may attain the size of a hen s egg or even of a large orange but many lead to a fatal outcome before they attain such dimensions The cavity contains thick greenish yellow pus which is often extremely fetid Commonly the abscess cavity is multilocular, and its interior is usually of a greyish green colour and covered with adherent purulent debris The abscess wall varies greatly in character with the age of the abscess In cases of recent origin there may be only a slight line of demarcation between the ragged, irregular cavity and the surrounding brain If the abscess has been present for a few weeks a well defined capsule can be seen and this can often be felt by the exploring cannula at operation In chronic cases the capsule may become so thick that the whole abscess can be shelled out of the brain without rupture The pus in such an abscess may become inspissated and sterile The white matter for a wide area surrounding an abscess is very œdematous and may contain areas of softening and fresh abscess formation The more acute the abscess the more marked is the surrounding œdema The surface of the brain overlying an abscess often shows a localised area of meningitis with flakes of purulent lymph adherent to the pia mater

The earliest stages of the development of a cerebral abscess seldom come under direct observation but there is every reason to suppose that the initial process is the development of an area of encephalitis around the nidus of invading organisms In *this area there is a mobilisation of inflammatory cells* with dilatation of capillaries and œdema Gradually liquefaction and pus formation take place in the centre while a fibroblastic reaction at the periphery gives rise to the abscess wall Outside this again is a neuroglial proliferation together with a diffuse inflammatory infiltration of the brain substance and perivascular spaces

Many cases of abscess are associated *with a terminal spreading meningitis* and in a proportion of cases rupture may have occurred either into the ventricles or the general subarachnoid space a complication which is invariably fatal within a few hours In adjacent abscesses it is not uncommon to find an associated subdural or extradural abscess which is invariably in direct contact with the primary focus of disease

Symptoms —A cerebral abscess has its origin in inflammation and constitutes when developed a foreign body within the skull Death may result from the effects

Abscesses situated in the parietal and occipital lobes are rare Except as a complication of osteomyelitis of the skull they are almost invariably metastatic in origin The most important local signs that they give rise to are contralateral sensory loss of a cortical type in the case of parietal lobe abscesses and defects in the contralateral fields of vision in those situated in the occipital region In either case epileptic attacks may occur

Cerebellar abscesses often present great difficulties in localisation The general symptomatology is much the same as in cases where the abscess is situated above the tentorium though on the whole the mental alteration is less and the vomiting and occipital pain more marked in cerebellar cases Nystagmus is a valuable sign which is seldom completely absent and some degree of weakness of a lower motor neurone type on the same side of the face is often present Both these signs however may be found in cases with a localised area of meningitis in the posterior fossa without any abscess within the cerebellum itself The most reliable sign is the presence of hypotonia and inco ordination of movement of the limbs on the same side of the body In bed these changes are most readily detected in the arms but if the patient is well enough to walk the inco ordination may be very evident in the gait It is by no means unusual for a cerebellar abscess to be present for many weeks without producing any detectable localising signs while the general condition of the patient leaves little room for doubt as to the presence of an abscess somewhere

The cerebrospinal fluid is very seldom completely normal in cases of cerebral abscess and examination of the fluid can afford very valuable aid in the diagnosis of doubtful cases Withdrawal of fluid is however by no means devoid of risk and may lead to a rapidly fatal result either by precipitating medullary failure or by causing the abscess to rupture into the ventricle For this reason when the diagnosis is not in doubt lumbar puncture should be avoided and when there is a suspicion that an abscess is present the smallest necessary quantity of fluid only should be withdrawn through a very fine needle The pressure of the fluid is raised and may reach a very high figure The first change to take place in the composition of the fluid is an increase in the amount of total protein from the normal 40 mg per cent to 60 or even 80 mg per cent With this is found a gradual increase in the number of cells to 10 or 20 and rarely more than 100 per c mm At first the cells are almost entirely lymphocytes though an occasional polymorph may be identified in a long search As the number of cells increases the proportion of polymorphs increases until they may constitute 10 per cent or even 20 per cent of the total Finally as the abscess approaches close either to the ventricle or to the convex surface of the brain such a brisk pleocytosis may be caused that the fluid becomes turbid in appearance but is still sterile with a normal or only very slightly reduced content of chlorides and sugar The finding of a turbid cerebrospinal fluid in which no organisms are seen and which remains sterile on culture is always extremely suggestive of a cerebral abscess

Diagnosis —The diagnosis of cerebral abscess has to be made from other complications of suppuration in the vicinity of the brain and from other expanding intra cranial lesions particularly cerebral tumour

The varieties of intracranial complication of neighbourhood suppuration most likely to be confused with cerebral abscess are

1 Acute spreading meningitis
2 Localised meningitis with or without an extradural abscess
3 Infective venous sinus thrombosis
4 Otitic hydrocephalus

1 *Acute spreading meningitis* —The differential diagnosis here seldom presents serious difficulty The high sustained fever rapid pulse delirium and marked neck rigidity all make the recognition of acute meningitis easy Difficulty does however,

normal rhythm of 70 to 80 per minute the pulse may often be found to fall progressively over days or weeks to 50 or fewer beats per minute With the bradycardia is *associated a similar but less striking fall in the* respiration rate

The mental state is often characteristic It is best defined as one of irritable drowsiness Left alone the patient will remain quiet for hours together with eyes closed only rousing occasionally to cry out with intense paroxysms of headache. Any attempt at examination is met by a fretful opposition and lack of attention which in the early stages are only too often thought to be due to sheer bad temper Mental slowness is more often met with in this than in any other intracranial disorder A question put to the patient may remain unanswered as if unheard for a minute or more and then just when it is about to be repeated a perfectly appropriate answer will be given in a petulant voice The patient may often be seen tentatively covering first one eye and then the other on account of double vision and in such cases an obvious internal strabismus may be present

The optic fundi in cases of cerebral abscess commonly show papillœdema if the condition lasts for more than a few weeks The swelling of the disks may come on with great rapidity and attain 3 to 4 dioptres of swelling with numerous hæmorrhages during the course of a few days It *not infrequently continues to increase in* severity for some days after the abscess has been drained and may even appear for the first time during this period Some degree of neck rigidity and a weakly positive Kernig s sign are not uncommonly met with particularly when the abscess is situated in the *cerebellum or when an appreciable degree of meningeal reaction is present* Local tenderness of the skull to firm pressure or percussion is a common finding and may afford valuable help in localising the abscess in doubtful cases The patient may rapidly become emaciated to a remarkable degree especially when the abscess is in *the cerebellum*

Localising signs will naturally vary with the position of the abscess Temporal abscess usually begins in the inferior portion of the lobe and extends upwards and forwards When situated on the left side in a right handed person one of the earliest *focal* disturbances to occur is disorder of speech At first this takes *the form of* difficulty then of inability to name objects correctly later difficulty in understanding spoken and written language and paraphasia make their appearance Naturally speech disturbances are not met with in right sided temporal lobe abscesses except in strongly left handed persons Another early sign of temporal abscess is disturbance of the contralateral fields of vision This nearly always takes the form of a congruous upper quadrantic hemianopia which gradually spreads to involve the lower quadrants until a complete hemianopia is present As the abscess extends forward towards the motor projection fibres weakness of the opposite side of the face of a supranuclear *type* develops to be followed by similar weakness of the contralateral arm and then of the leg until a complete hemiparesis may be present with characteristic increase in the tendon reflexes diminution or loss of the abdominal reflexes and an extensor plantar response Contralateral sensory disturbances may be met with but they are late to appear and by no means common Epileptic disturbances may occur in temporal lobe abscesses and when these are deeply situated the fits may assume a characteristically uncinate form

Abscesses in the frontal lobes are on the whole more silent than *those in the* temporal lobes Whether adjacent or metastatic in origin they usually originate well forward in the prefrontal areas and may attain a very large size without producing any localising signs whatever Mental change of the kind already mentioned may be an unduly conspicuous feature Apathy and forgetfulness may be marked and an early loss of sphincter control may be noted As the abscess extends backwards towards the motor area a contralateral hemiparesis develops involving face and arm before the leg and if the lesion is on the left side an increasing degree of executive aphasia may be in evidence in normal persons *Epileptic fits are not uncommon*

the past the recovery rate has been low but with modern neuro surgical technique a high proportion of recoveries can be obtained Unfortunately epileptic fits subsequently occur in approximately 50 per cent of cases recovering from cerebral abscess

(2) ENCEPHALITIS LETHARGICA (see p 1414)

(3) ENCEPHALITIS ASSOCIATED WITH ACUTE SPECIFIC FEVERS

Ætiology —Acute encephalitis may occur as a rare complication of a number of acute specific fevers especially of the exanthemata In some cases the brain alone may be involved but in others the nervous system may be more widely affected and *the picture is rather that of an encephalomyelitis* The fevers most commonly associated with this complication are measles and vaccinia but it occurs also with variola scarlatina mumps and varicella and many other acute febrile disorders The incidence of encephalic complications of these diseases varies noticeably from time to time

The exact relationship of the encephalitis to the preceding infection is by no means clear nor is it certain that the cerebral complications of the different exanthemata are identical The hypothesis that the exanthem merely serves to activate some unknown causative agent such as a latent virus is without confirmation It must also be borne in mind that all cerebral complications of acute fevers are not necessarily encephalitic but may result from vascular occlusion by thrombosis or embolism or from hæmorrhage or from meningitis

Pathology —In a great many cases recovery ensues and the pathology of the condition remains unknown A considerable number of cases of measles and vaccinial encephalitis have however been subjected to full pathological examination and have shown a fairly constant condition of the nervous system and the much rarer examples following other fevers have generally conformed to this picture The brain and spinal cord show diffuse congestion particularly of the white matter sometimes causing petechial hæmorrhages Numerous areas of acute demyelination occur particularly in the perivascular zones These are so constant as to have suggested the title perivascular myelinoclasis (Hurst) for this group of disorders In addition there is a marked perivascular infiltration with round cells and a more diffuse cellular reaction in the nervous tissue with mobilisation of microglia and proliferation of the astrocytes

Symptoms —The time of onset of encephalic symptoms is fairly constant in each exanthem In measles it is commonest towards the end of the first week in vaccinia from 10 to 14 days after the vaccination and in variola during the second week of the eruption Common symptoms are drowsiness increasing in severe cases to coma headache convulsions cranial nerve palsies dysarthria and dysphagia and in some cases myoclonic or choreiform movements Slight signs of meningeal irritation such as neck rigidity irritability and photophobia may occur and there may be an increase in the fever Papillœdema may develop In cases associated with myelitis marked weakness in the lower limbs with retention of urine is common Loss of the abdominal reflexes and extensor plantar responses are frequent The cerebrospinal fluid is commonly under increased pressure and shows an increase in protein content with a mild lymphocyte pleocytosis (10 to 50 per c mm) The Lange colloidal gold reaction may be strongly positive and sometimes paretic in character The content of sugar and chlorides is normal

Diagnosis —The occurrence of symptoms of this order at the significant period of the different diseases makes the diagnosis in most cases clear It should be remembered however that acute fevers in children may determine the moment of onset of tuberculous meningitis and that vascular disorders may occur in a similar setting

Prognosis —In cases which do not succumb to coma or convulsions during the first week recovery is the rule and is usually remarkably complete Residual paralyses

arise when a cerebral abscess is causing a brisk meningeal reaction and actual infection of the subarachnoid space is imminent In such cases the symptoms and signs of the two diseases are likely to be superimposed on one another The finding in such cases of a turbid fluid without visible organisms which is sterile on culture with normal salt and sugar content is very suggestive of an abscess with an acute meningeal reaction

2 *Localised meningitis* —This condition often affords the most difficult problem in the differential diagnosis of cerebral abscess In the presence of an acute infection on the outer aspect of the dura, especially if there is an extradural abscess as is so often the case in mastoid disease it is not surprising that there should be a brisk local inflammatory reaction of the leptomeninges on the inner aspect of the dura This local area of meningitis may produce the same local symptoms and signs as an abscess in the same locality and if it involves the base of the brain may also give rise to all the signs of raised intracranial pressure by obstructing the normal circulation of cerebrospinal fluid In otitic cases this is particularly likely to occur in the posterior fossa thus simulating a cerebellar abscess On the whole such cases come on more rapidly than abscesses and the symptoms and signs are more fluctuant The tempera ture is usually higher and the pulse rate more rapid than in abscess and the signs of meningeal irritation more marked The central nervous signs are those which might be expected to result from a lesion on the surface rather than in the substance of the brain for example cranial nerve palsies There seems every reason to suppose that in some cases this localised meningitis is capable of undergoing complete resolution especially since the introduction of antibiotics On the other hand it may be but the prelude of a general meningeal spread

3 *Infective venous sinus thrombosis* —This condition seldom resembles cerebral abscess sufficiently closely to present serious difficulty in diagnosis It is character ised by high, swinging fever with frequent rigors intense toxæmia and the other evidences of a pyæmic state There are no signs indicative of raised intracranial pressure or of local disturbance of brain function

4 *Otitic hydrocephalus* (see Hydrocephalus pp 1399 and 1404) —Otitic hydro cephalus is a condition almost confined to children and adolescents It is character ised by the symptoms and signs of raised intracranial pressure including papillœdema without signs of focal damage to the brain Its onset is more acute and the symptoms more violent than in cerebral abscess and the patient s general condition between paroxysms of headache remains remarkably good Apart from an increase in its pressure and quantity the cerebrospinal fluid is quite normal

Cerebral abscess may be distinguished from cerebral tumour by its association with suppurative conditions elsewhere in the body the rapid increase in symptoms the general reaction of the patient and the changes in the cerebrospinal fluid In spite of these criteria chronic cerebral abscesses are not infrequently operated upon in the belief that they are true neoplasms

Course and Prognosis —The natural termination of a cerebral abscess which is not drained is in the vast majority of cases the death of the patient Cases of spontaneous evacuation of the pus through the ear or nose are recorded in the litera ture and in a small number of cases the pus becomes inspissated and the capsule so enormously thick that the abscess may lie dormant in the brain for many years and become calcified Such abscesses may later be removed bodily as encapsuled ' tumours , the nature of which is only discovered after section Death takes place from the results of raised intracranial pressure from acute meningitis from spread of the infection to the general subarachnoid space or from rupture into the ventricle

Treatment —*The treatment of cerebral abscess is surgical* The condition is one of the greatest urgency as death may occur at any moment Surgical treatment should only be entrusted to an experienced neuro surgeon and direct drainage through the portal of entry *e g* the middle ear or frontal sinus carries a high mortality In

has been the first symptom and is the result of the symmetrical demyelination of the occipital white matter As the disease spreads forwards into the temporal regions bilateral deafness appears and later bilateral ataxy and astereognosis—due to parietal involvement bilateral spastic paralysis—the result of central involvement, and complete amentia—due to callosal and prefrontal involvement develop

In those cases in which the initial seat of the disease is in the temporal central or frontal regions the first symptom to appear is obviously determined by the location and the order of development of symptoms will be changed but the mode of progress is the same in all Where the disease starts on one side only hemianopia or hemiplegia is the first symptom and these are followed by the train of added signs produced by the extension of the disease into other regions Complete mindlessness and paralysis always dominate the clinical picture in the end The disease process within the brain sometimes causes swelling with increase of intracranial pressure and signs of the latter may appear in the form of headache, vomiting and papillœdema Such cases are not common and most of them have been regarded in life as cases of intracranial tumour Fits are by no means uncommon Sometimes they constitute the initial manifestation of the disease and they may occur at any time during its course and may be local or general Fever is usually absent but there may be irregular pyrexia and some of the more acute cases have been pyrexial throughout The cerebrospinal fluid is normal in the majority of the cases but sometimes there is an increased protein content and a small excess of lymphocytes

Diagnosis —The onset with cerebral blindness or with bilateral deafness followed by signs of progressive cerebral destruction is so rare in any other disorder as at once to suggest the diagnosis of Schilder s disease indeed no less than two thirds of the reported cases have shown this picture When the disease begins unilaterally and more particularly when headache vomiting and papillœdema are present the distinction from intracranial tumour is difficult or even impossible for in both diseases the local commencement and the progressive destruction occur In Schilder s disease however high grade papillœdema is not met with and consecutive optic atrophy does not occur It should be borne in mind that any locally commencing progressive destruction of the brain may be an example of this malady

Course and Prognosis —In most cases Schilder s disease is regularly progressive to a fatal termination In some however periods of standstill have been noted while in a few others marked improvement for a time has occurred The duration has varied from 7 days to 36 months with an average of 9 months

Treatment —No treatment is at present known that will influence the course of this disease

(5) SUBACUTE INCLUSION BODY ENCEPHALITIS

In recent years a type of subacute encephalitis at present only observed in children and adolescents has been reported by Dawson Van Bogaert Greenfield and others

Pathologically it is characterised by the presence of inclusion bodies in the nerve cells generally regarded as the hallmark of virus diseases together with polioclasis and neuronophagia

Together with this is a degree of demyelinisation and sclerosis of the white matter reminiscent of the leuco encephalitides of the Schilder type

Clinically the disorder runs a progressive subacute course towards a fatal termination The earliest symptom is usually mental deterioration often associated with epileptic manifestations Later involuntary movements of various kinds occur and the child gradually develops the picture of bilateral rigidity of extrapyramidal type with relatively few pyramidal signs until death occurs at a stage of profound dementia with akinesis and contractures

are exceptional In a small number of cases some residual intellectual impairment may result and in other cases a liability to fits The mortality in vaccinal cases is from 25 to 40 per cent , that in measles and the other common exanthemata very much lower

Treatment —This is symptomatic There is no evidence that specific antisera when available, affect the course of the nervous complications

(4) SCHILDER S DISEASE

Synonym —Encephalitis Periaxialis

Definition —A malady characterised anatomically by a progressive and massive demyelination of the white centres of the cerebral hemispheres, proceeding from a *single focus or from two symmetrical foci, and producing the clinical picture of* progressively increasing failure of cerebral function local at first but advancing in terms of the functions of the contiguous regions which are next affected, by the spread of the disease from its starting point

Ætiology —Nothing is known *of the essential nature of the disease,* nor is it certain that all cases included under this heading form a homogeneous group Origin ally regarded as an inflammatory probably an infective, disease the increasing evidence of its familial incidence suggests that it may be primarily degenerative It has also been suggested that those cases in which an inflammatory reaction is present may be infective and those in which it is absent—as it may be—degenerative Many of the reported cases have occurred in childhood even as early as the second year The latest case was in the fifth decade of life The sexes are equally affected

Pathology —The characteristic lesion consists of (1) A primary demyelination and later, destruction of the axis cylinders of the central white substances of the cerebral hemispheres which till very late spares the subcortical zone of white fibres and the radial cortical fibres and produces a translucent jelly like appearance of the oval centres (2) A very early and perhaps primary overgrowth of the neuroglia forming a *feltwork,* which is particularly intense round *the vessels (3) A general* infiltration of the white matter of the brain with round cells most of which are engaged in the removal of altered myelin or in the formation of neuroglial fibres

The process commences most commonly as symmetrical patches of demyelination in *either occipital white centre* less *frequently in both temporal white centres* or in both prefrontal white centres, and spreads directly thence until the whole of the oval white centres becomes demyelinated The corpus callosum is involved and the demyelination spreads downwards through the crura into the brain stem Sometimes especially in the central regions the disease starts on one side and after playing havoc with the white centre of one hemisphere spreads across the corpus callosum into the other The resulting picture of a brain normal on the surface and on section with apparently normal cortex and intact subcortical white bands but with the oval centre completely changed and translucent, is peculiar to this disease Not infre quently other patches *of the disease may be scattered throughout the central nervous* system. This scattered distribution and the prominence of demyelination bring Schilder s disease very close to disseminated sclerosis and it has actually been de scribed as disseminate sclerosis in childhood but the massiveness and mode of *spread of the lesions together* with their distribution with predilection for the brain and avoidance of the spinal cord its incidence in childhood and its entirely different symptomatology separate Schilder s disease sharply from di seminated sclerosis It is largely to Collier that we owe the clinical recognition of this malady

Symptoms —The clinical aspect is precisely that which might be expected from a progressive destruction of cerebral function spreading by contiguity from *the initial seat of the disease* In many of the cases blindness—by which is meant blind ness without any change in the optic disks and with pupils reacting normally to *light*—

in the seventh decade of life but it was rare in young children and seemed to be most incident in the first half of adult life The mode of infection is unknown According to von Economo when once the virus obtains access to the nervous system it spreads as in other cases of virus diseases of the nervous system by axonal routes Its effect remains confined to the nervous system but the occurrence of progressive nervous sequelæ long after the acute illness which is such a marked characteristic of the disease suggests that the virus may survive in the nervous system for long periods of time

The height of the epidemic incidence of lethargic encephalitis has many times coincided with a severe epidemic of influenza but no further connection between the two conditions is known Claimed at one time as an aberrant form of poliomyelitis infection von Economo s disease has proved quite distinct both in its age incidence seasonal prevalence morbid anatomy and symptomatology Economo first succeeded in transferring the disease to the monkey by intracerebral inoculation in 1916 Subsequent smaller epidemics in Japan and St Louis though conforming in general to the features of the pandemic of 1917–1920 have shown sufficiently constant variation in age incidence and death rate as well as clinical feature to make it seem likely that there exist more than one strain of the virus

Pathology—The pressure and quantity of the cerebrospinal fluid are always increased and in a few of the cases blood or the products of hæmorrhage are present In about one third of cases the cell count has been normal In the rest there has been a moderate lymphocytic pleocytosis with little or no protein increase the titre of the sugar tending to a high normal and that of the chlorides being normal No prognostic indications can be derived from the nature of the fluid The vessels of the brain are markedly congested and full of blood and the colour shows a characteristic change from the normal throughout the whole of the grey matter varying from a rosy flush to a deep salmon pink giving rise to the term the rose coloured brain When hardened in formalin this colour becomes a heavy purple grey Both subdural and deeply seated hæmorrhages are occasionally found Economo describes the anatomical picture as one of unvarying constancy It is that of an œdematous and congested brain with all the grey matter conspicuously reddened in contrast to the white matter which is of normal colour There is a non purulent and properly speaking a non hæmorrhagic inflammation of the whole grey matter exclusively, the white matter being uninvolved There is most conspicuous perivascular lymphocytic cuffing remarkable for the absence of any polymorphs with an intense cellular infiltration of the grey matter with elements of the microglia while the neuroglia is unaltered and demyelination does not occur Accompanying and succeeding these inflammatory changes is a certain measure of neuronophagia with primary loss of the ganglion cells

Symptoms—In the acute forms of the malady the onset is often ushered in by general symptoms such as shivering malaise headache and fever and bodily pains a thickly coated white tongue and constipation and sometimes vomiting and persistent hiccough This train of symptoms usually appears in the story as an attack of influenza The pyrexia does not usually last longer than a week Countless such attacks of influenza distinguishable only by the occurrence of transient diplopia or of slight somnolence and often even without any such distinguishing features have been completely recovered from at the time but have been followed after long intervals by the slow onset of the Parkinsonism of lethargic encephalitis Again the epoch of infection may apparently give rise to no symptoms at all and long afterwards an insidious onset of Parkinsonism ensues

The Nervous Signs—*Mental symptoms*—An increasing lethargy which often becomes very deep is present in many of the cases In this condition the patient will lie for days without stirring a muscle taking no heed of his surroundings and passing the dejecta under him unheeding Yet when roused by command and

VIRUS DISEASES OF THE NERVOUS SYSTEM

Certain viruses have a selective affinity for the nervous system and are therefore spoken of as neurotropic They act upon the nerve cell, and to a less degree upon glia cells, but not upon the white matter They are capable of multiplication and of exerting their pathogenic action only within the nerve cell where their life and activity are short lived

The essential lesion resulting from their presence is an acute necrosis of the nerve cell leading to the death and destruction or to the damage of the cell A secondary glial and vascular reaction ensues as a result of which lymphocytes pass into the cerebrospinal fluid from the perivascular spaces in the affected regions of the nervous system

The so called post infective encephalitis that may follow the acute exanthemata has not the pathological characters common to the proved virus infections of the nervous system since the lesion is one of demyelination and not an attack upon the nerve cell The nature of this form of encephalitis remains obscure (see p 1411)

ENCEPHALITIS LETHARGICA

Synonym —Epidemic Encephalitis

Definition —An acute febrile disease occurring sporadically and epidemically due to the infection of the nervous system by a virus which has not yet been identified but which can be inoculated into the nervous system of monkeys reproducing the disease The malady has its principal incidence upon the upper parts of the nervous system the cerebrum basal ganglia and brain stem Though very definite it is remarkably polymorphic, and it is sometimes mono symptomatic, and its type has changed greatly during the passage of an epidemic The absence of evidence of case to case infection has necessitated the assumption that infection is transferred by carriers or by those in the pre symptomatic stage of infection only

History —When we read of the influenza epidemic which swept over Europe in 1580 and which was accompanied by a malady so peculiar as to gain the title of ' schlafkrankheit , and afterwards of the epidemic described by Sydenham in 1675 as febris comatosa the sleeping sickness of Tubingen in 1712 and Dubini s epidemic of the fatal electrical chorea in Northern Italy in 1846 we cannot but agree with von Economo s conclusion that these epidemics were epidemics of lethargic encephalitis The subsequent epidemics of Mauthner s Nona in Piedmont in 1891 and also Pfuhl Leichtenstern s hæmorrhagic encephalitis in 1905 have been shown to be similar to lethargic encephalitis both clinically and pathologically The malady last became pandemic in Britain and Northern Europe from 1917, reaching a maximum in 1920 and then declined almost to vanishing point over the next 15 years

In this country sporadic cases of sufficiently definite characteristics to stand up to both clinical and pathological criteria of diagnosis have continued to make their appearance but they are rare *It should be remembered that many cases thought* to be of this nature prove at autopsy to be due to tumours or other causes On the other hand the continued appearance of cases of Parkinsonism in young people not infrequently associated with other post encephalitic sequelæ makes it seem likely that instances of the infection so mild as not to produce clinically recognisable symptoms are not infrequent

Ætiology —During the period of its frequent incidence the disease occurred both sporadically and epidemically with no centre of spread It was more prevalent in the cold season of the year No age was exempt from the malady and cases occurred

stiff the arms held away from the trunk the whole appearance of the patient closely resembling that of paralysis agitans Rapid fluttering of the eyelids when gently closed is characteristic of this condition The spontaneous involuntary movements may be of a rhythmic tremulous nature as in paralysis agitans or there may be slow rhythmic choreiform athetoid myoclonic irregular or highly complicated movements these may be met with at any stage of the malady but most commonly appear some little time after the acute stage has passed away Fibrillation and fascicular twitching of the muscles is very common in the acute stage In cases where bulbar symptoms either of a spastic or flaccid kind are present hypersalivation of the nature of a true sialorrhœa is often a most troublesome symptom

In addition to the above common symptoms and signs other indications of involvement of the cerebral hemispheres may occur Bilateral spasticity with signs of involvement of the pyramidal systems increased jerks lost abdominal reflexes and extensor plantar responses are common Hemiplegia aphasia and hemianopia may occur Meningeal symptoms may be very marked in the early stages such as suboccipital headache painful stiffness of the neck head retraction vomiting and Kernig s sign Indeed rapidly fatal cases have occurred in which the clinical picture throughout was hardly distinguishable from that of acute meningitis but without any leucocytosis in the cerebrospinal fluid A major incidence of the lesions upon the cerebellum gives rise to the picture of acute cerebellar ataxy following a lethargic onset, and the end result may be a condition closely resembling a usual type of disseminate sclerosis Such cases make a good recovery in the course of time

Peripheral pains are sometimes very severe and are usually quite local They may be the first signs of the illness and may persist for months after recovery They are presumably due to the lesions around the nerve roots which have been already referred to

Spinal symptoms —Since lesions have been found in the spinal cord it is only to be expected that focal spinal symptoms should be met with in rare cases These are usually acute atrophic paralyses similar to those of poliomyelitis and recover completely It has been argued however that this atrophic palsy is due to a lesion of the spinal roots More severe lesions may apparently give rise to a condition resembling acute transverse myelitis

The incontinence which is almost constantly present even when the lethargy is far from deep is the result of the lethargy Transient conscious dysuria is however not infrequent in the early stages of the disease The deep reflexes may be lost in severe cases during the acute stages and they are usually absent in premortal conditions Otherwise they tend to be exaggerated especially if involvement of the pyramidal system be present The condition of the abdominal and plantar reflexes depends upon the presence or absence of lesions affecting the pyramidal tracts In the former case the abdominal reflexes will be absent and the plantar reflexes of the extensor type

Attention must be drawn to a group of cases in which the initial manifestations of the disease are so slight as not even to interfere with the daily work or to call for medical attention and yet in the course of months or it may be even years the most serious and completely incapacitating paralysis appears Such a patient may notice that he sees double and does not feel very well for a few weeks He recovers but after a few years begins to manifest the signs of a slowly oncoming Parkinsonism A similar result in the slow and late development of grievous symptoms may follow any attack of lethargic encephalitis and make the prognosis in this malady very difficult.

Sequelæ —The disabilities which this malady may leave in its wake are numerous and varied The mental paralytic and Parkinsonian end results have already been referred to but special mention must be made of the so called oculogyric crises and of involuntary spontaneous movements having the general features of habit spasms or tics

vigorous bodily stirring he will wake up and hold a very intelligent conversation, lapsing back at once when he is left alone even though his mouth be half full of unswallowed food In this condition flexibilitas cerea may often be demonstrated in the limbs The lethargy may last for 3 weeks or longer even in patients who completely recover It passes away gradually Unrousable coma is invariably a sign of impending dissolution Subsequent memory of events during the early days of the lethargy may be remarkably retained Insomnia may be a troublesome early symptom, and even when the patients are markedly lethargic they will complain that they cannot sleep *Occasionally reversal of sleep rhythm may occur, the patient sleeping soundly* all day only to become restless and overactive at night Lethargy however may be completely absent and the early mental state be that of vivacious excitement and talkativeness Irritability and restlessness may be present In some cases the first nervous sign may be delirium or mental aberration, which may rapidly develop into acute and violent mania such cases are rapidly fatal In cases which recover after severe symptoms considerable mental reduction and self obvious mental change may persist Indeed it has been said that no sufferer from this disease ever regains his original mentality, and it is a common experience to find the personality very seriously changed in the way of mental reduction Complete incapacity for any sustained work entire change of character anti social tendencies moral perversion and depressed neurasthenic states are not uncommon sequels of the disease, particularly when it occurs in children or adolescents (see also p 1634)

Convulsions are very rare but they may undoubtedly occur as in other forms of encephalitis Indeed the initial clinical picture may be dominated by convulsion and closely resemble status epilepticus from other causes

Ophthalmoplegia and other paralyses in the region of the cranial nerves are most often nuclear in type but peripheral paralysis of any cranial nerve may be met with most commonly unilateral paralysis of the facial nerve The pupils may show every abnormality which a lesion of the nervous system can produce Inequality unroundness eccentricity and loss of light reflex and ciliary paralysis may occur The loss *of light reflex may be unilateral The external ophthalmoplegia* being nuclear in origin, involves both eyes in terms of their conjugate movements and the upward and downward movements are as a rule more severely impaired than are the lateral movements '*Bilateral* ptosis is very usual and is a most important and valuable early indication of the disease' The common error is to consider it part of the sleepy state The nuclear ophthalmoplegia is often irregular giving rise to strabismus and diplopia Either in addition to the above or existing alone there may be peripheral paralysis of any of the oculo motor nerve trunks The degree of the ophthalmoplegia varies in different cases from slight diplopia with hardly noticeable strabismus to complete paralysis of both eyes It may be rapidly transient or permanently severe In severe cases which survive there is always some improvement in the degree of paralysis in the course of time

Vision—The diplopia and loss of accommodation cause much defect of vision but *many of the patients complain of a loss of vision in each eye* which is too great for any such explanation the cause of which is not yet explicable Papillœdema has been reported in a few cases It is transient and never reaches a high degree

Bilateral nuclear facial paralysis and bulbar paralysis are not uncommon Paralysis of any individual cranial nerve may occur, and also of any individual spinal root Such paralyses always completely recover in the course of time

Symptoms indicative of lesion of the basal ganglia are among the most common features of the disease and they are often the most persistent These consist of weakness of movement rigidity with slowness of movement and spontaneous involuntary movements The weakness rigidity and slowness of *movement give* rise to a peculiar immobility of facial and bodily expression and movement The face is mask like the neck stiff and the head moves little and slowly the trunk bent forward and

favour of survival The prognosis however as to how much permanent damage to the nervous system will eventually remain is hardly possible since slow improvement may go on for months and even years Of the acute cases occurring at the height of an epidemic, 40 per cent are quickly fatal 30 per cent are reduced to chronic invalidism and 30 per cent appear to recover completely (Economo) In most of these latter the syndrome of Parkinsonism subsequently appears after an interval which may be a few months or many years and the weakness rigidity and tremors which form this paralysis agitans like picture persist indefinitely

Treatment—Nothing being known of the infectivity and mode of spread of the disease isolation and disinfection are not usually employed Each case must in England be immediately notified to the public health authorities No treatment is known which has any specific influence upon the disease Intravenous injection of collosol iodine solution (150 ml for a dose) repeated on the second and fourth days has been advocated and is certainly without harmful effects but there is little evidence that it is of value There has as yet been little opportunity to investigate the effects of antibiotics It remains therefore to use those measures which will help to keep the patient alive and those which relieve symptoms Nasal feeding may be necessary Relief of the constipation is most important and is often followed by striking improvement in the symptoms After the acute stage treatment is concerned with combating the physical and mental listlessness and depression which so often persist and with the restoration of normal mobility and function to the limb In these physical and occupational therapy can play a useful part

HERPES ZOSTER

Synonym—Zoster Shingles

Definition—An acute infection of the posterior root ganglion by a neurotropic virus leading to severe pain in the distribution of the corresponding posterior root and to the appearance of a crop of vesicles in the cutaneous distribution of the root

Ætiology—The virus of zoster stands in some as yet undetermined relation to that of chicken pox and the appearance of the latter malady in a susceptible subject some 14 days after contact with a case of zoster has been too frequently recorded to be of the nature of coincidence

The disease is seen at all ages but according to Head is perhaps most common in adolescents In elderly patients it is frequently a more serious as well as a more painful affection than in young persons It may arise without discoverable cause and with a febrile reaction and considerable malaise It may also occur apparently symptomatically during the course of arsenical medication or during such illnesses as pneumonia tabes dorsalis and tuberculosis

Pathology—The essential lesion is an acute inflammation of the dorsal root *ganglion of the same histological character as the lesion of acute anterior poliomyelitis* There are degenerative nerve cell changes with accompanying microglial reaction and perivascular infiltration with round cells Later degenerative changes occur in the fibres of the dorsal roots and of the peripheral sensory nerves The Gasserian ganglion and the thoracic and upper two or three lumbar ganglia are most often affected There is an increased protein and lymphocyte count in the cerebrospinal fluid

Symptoms—There may be an onset with fever which persists for 2 3 or even 4 days There is from the first pain at the place at which later the herpetic eruption is to appear This occurs on the third or fourth day of the illness At first the rash is a patchy erythema upon which appear small vesicles filled with clear fluid From the fifth to the tenth day the vesicles dry up and shrink progressively until a scab is formed This finally drops off sometimes leaving considerable scarring These

Oculogyric crises —This term is applied to recurring attacks of tonic conjugate deviation of the eyes This is almost always upwards and is accompanied by wrinkling of the forehead extension of the neck and in fact all the muscular activity associated with the act of looking upwards Deviation of the eyes to one side is exceedingly rare The attacks may occur several times a day or only at an interval of months They are often very specific in their times of occurrence and may be precipitated by a variety of stimuli such as emotion fatigue or watching a moving picture The attack may last from a few minutes to many hours and often passes off only after sleep It is commonly associated with an intense degree of mental depression and while it lasts the patient may experience recurring obsessional thoughts be impelled to carry out stereotyped movements or develop ideas of reference, particularly feelings of *persecution*

Patients suffering from oculogyric crises always show some signs of Parkinsonism. The attacks often gradually grow less frequent over a period of years and may cease completely Their frequency and duration is in many cases considerably reduced by the regular administration of amphetamine sulphate 5 to 10 mg twice daily

Post encephalitic tics —A great variety of stereotyped involuntary movements are met with in post encephalitic subjects usually in association with some degree of Parkinsonism Rhythmic movements of the jaws tongue and face are common. Alterations in respiratory rhythm with sighing gasping inspirations may occur Torticollis indistinguishable from the variety met with in elderly subjects is not rare and there may be hideous recurring contortions of the face and trunk and most grotesque mannerisms of gait and speech

Diagnosis —A diagnosis of lethargic encephalitis is not infrequently made but must be received with the very greatest reserve at the present time Under this title *most neurologists have encountered a great variety of nervous disease including intra* cranial tumour, cerebral abscess, subdural hæmatoma tuberculous meningitis and the like In typical cases the diagnosis presents no difficulty, the rousable lethargy incontinence ophthalmoplegia and negative lymphocytic or blood containing cerebro spinal fluid being so characteristic as to preclude possibility of error The less usual forms of the malady and especially those with very gradual onset and slight symptoms often present great difficulty and require much care and full knowledge of the possible symptomatology of the disease for their recognition There is no specific laboratory test for the malady and the diagnosis must be based upon clinical grounds Where meningeal symptoms are prominent distinction has to be made from other forms of meningitis and from poliomyelitis Here the cerebrospinal fluid is of the highest importance as polymorphonuclear leucocytes occur very rarely in lethargic encephal itis In cases commencing with peripheral pains excitement maniacal symptoms or convulsions careful lookout should be kept for the advent of ptosis ophthalmoplegia or lethargy the appearance of which following such symptoms should at once suggest the diagnosis It must be borne in mind that the clinical picture of the disease may be dominated by a hemiplegic condition, and that an apoplexy may occur during the acute stage of the disease Slight cases of the disease are frequently unrecognised or are indeed unrecognisable in the early stages but here the diagnosis can often be *made with certainty from the end results the peculiar ophthalmoplegia* the spon taneous involuntary movements and the paralysis agitans like syndrome being almost pathognomonic of the malady

Course —The course of the disease is extremely variable It may be a slight transient illness lasting but a few days and leaving no sequelæ after a few weeks or a most malignant disease *fatal in a few days In others symptoms* indicative of fresh lesions may occur repeatedly weeks and even months after the onset

Prognosis —A rapid onset and quick development of severe symptoms marked pyrexia delirium and maniacal excitement are bad prognostic signs and indicate a rapidly fatal issue After the third week of the disease the probabilities are all in

Ætiology —The disease is generally transmitted either by the licking of a freshly abraded surface of skin or the bite of an infected dog In Eastern Europe and the Orient wolves not uncommonly transmit the disease and owing to extensive laceration of the tissues a greater proportion of people bitten by them develop the disease than with either dogs or jackals It has been estimated that wolf bites entail a mortality of 80 per cent In Trinidad in 1925 an epidemic of paralytic rabies in man was attributed to the bites of vampire bats cattle being the original source of infection

The virus of rabies —This belongs to the class of neurotropic viruses that have a special affinity for attacking the grey matter of the nervous system

Pasteur in 1881 discovered that rabies could be transferred in series from animal to animal by subdural inoculation of emulsions of central nervous tissue derived from an infected dog In rabbits after some twenty passages the virus became modified firstly the incubation period of ordinary street virus which varied from 8 to 60 days was reduced to 7 days and secondly it lost its capacity to reproduce the disease on subcutaneous inoculation Such a virus is known as fixed virus or virus fixé Street virus on the other hand is transmitted from the local wound via the peripheral nerves to the central nervous system and if the sciatic nerve be inoculated the lumbar cord becomes infectious several days before the virus can be demonstrated in the brain (di Vestea and Zagari) This accounts for the fact that cases bitten about the face head and neck have such a short incubation period The virus is destroyed at 50° C and is attenuated by drying—a fact made use of in the preparation of antirabic vaccine by the Pasteur method

Pathology —Excess of cerebrospinal fluid petechial hæmorrhages of the pia arachnoid and injection of its vessels may be found at autopsy Histological examination reveals cellular infiltration of the perivascular lymph spaces as well as Negri bodies within the cytoplasm of the nerve cells and their processes These bodies were described by Negri in 1903 They are globular or ovoid structures of variable diameter (0 5 to 25 0 microns) and are especially common in the Purkinje cells of the cerebellum and the hippocampus These inclusion bodies are present in the brain of 97 per cent of dogs infected with street virus

Symptoms —The period intervening between the bite and the clinical manifestations varies from 1 to 2 months as a rule the limits being 11 days to over a year Face head and neck bites have a shorter incubation period than those on the upper extremity and arm bites a shorter incubation than those implicating the leg The onset is generally sudden but prodromal symptoms are sometimes noted for a day or two before a hydrophobic syndrome appears For convenience three stages are described

1 *The invasion stage* —This includes prodromal features such as pain in the scar fever headache rapid pulse anxiety restlessness insomnia irregular and sighing respirations and phases of rushed speaking

2 *The stage of excitation* —This supervenes in 24 to 48 hours There is intense restlessness mental excitement hyperæsthesia and hydrophobia which consists of a sudden spasmodic spasm of the muscles of the mouth pharynx and larynx and to a greater or lesser degree the whole respiratory musculature A typical attack may be induced by offering the patient water As the glass approaches the mouth the head retracts in a series of spasmodic jerks associated with gasping respirations while any water reaching the mouth is immediately ejected The shoulders are elevated the chest expanded and the sterno mastoid and platysma muscles contracted Later the synaptic resistance in the reflex arcs become so lowered that a variety of sensory stimuli such as a sudden sound cold air strong light a strange smell and even the suggestion of water may suffice to induce the attack The voice is altered Frothy saliva collects in the throat and mouth and is flung off the lips during the attacks which may be characterised by intense fury or the most profound terror Lastly opisthotonus and general respiratory spasm are superadded In the interval the mind

scars may be anæsthetic to touch pinprick and temperature sense The pain before and during the evolution of the cutaneous lesion may be intense It is of a burning and itching quality, and in frail and elderly persons it may persist as a most intractable post herpetic neuralgia for months or even years

Herpes of the ophthalmic division of the fifth nerve is most commonly found in elderly persons Corneal vesicles may form and burst giving rise to ulcers which may spread and end in residual scarring (nebulæ) which impairs vision

Herpes of the geniculate ganglion occasionally occurs The vesicles are found in the pinna and there is pain in this region over the mastoid, and sometimes in the fauces (see pp 1248 1346)

Localised paralysis may accompany herpes Thus in ophthalmic herpes there is occasionally third nerve palsy, with ptosis and squint In geniculate herpes facial palsy with loss of taste over the anterior two thirds of the tongue is the rule In *herpes of the lower thoracic ganglia there may be paralysis of the oblique abdominal* muscles on the affected side The marked local bulging of the abdominal wall which ensues resembles at first sight the presence of an abdominal tumour These paralyses do not invariably clear up though the facial palsy of geniculate herpes does so more frequently than the paralysis of the abdominal muscles

Treatment —The course of the cutaneous lesions is not influenced by treatment which is directed to keeping the vesicles dry and free from infection For this purpose a dusting powder of starch or zinc oxide, or a collodion dressing may be used

During the acute stage pain may be relieved by aspirin or phenacetin but the post herpetic neuralgia so often met with in elderly patients may prove intractable and so severe as to render life scarcely tolerable It consists of a persistent burning soreness often associated with numbness and dysæsthesia over the area previously effected by the eruption

This pain is aggravated by fatigue worry and physical debility and often induces a neurotic reaction on the part of the patient or a state of depression in which suicide may be contemplated

Both analgesics and hypnotics are commonly needed over a period of many months The former may profitably take the form of some such mixture as the following tinct gelsemi min 10 phenazone gr 10 phenobarb sod gr ¼ Aq chlorof ad fl oz 1 t d s For the latter one of the short acting barbiturates is to be preferred A word of caution should be given against the dangers of excessive sedation in elderly subjects especially with bromides as a toxic confusional state is easily produced

A great variety of local applications have been used without avail Surgical measures such as division of peripheral nerves posterior spinal roots or the spino thalamic tract in the cord are equally ineffective As a last resort in the elderly depressed subject frontal leucotomy may be justified and while it does not remove the unpleasant sensation it allays tension and depression and frees the patient's mind from perpetual preoccupation with the pain which is one of the most noticeable features of this distressing malady

RABIES

Synonyms —Hydrophobia Lyssa

Definition —This is an infective disease due to a filtrable virus which is located in the salivary glands and central nervous system It is transmitted to man and most warm blooded animals through infective saliva of canines or blood lapping bats There is a long and variable incubation period and a short pyrexial illness of sudden onset characterised by fever nervous exaltation and violent muscular spasms involving the œsophagus and respiratory system *Once symptoms have supervened* the patient invariably succumbs

rabies prophylactic inoculation need not be advised unless fresh skin abrasions were present at the time.

Local treatment—If seen within 30 minutes bleeding should be encouraged by the application of a ligature just tight enough to obstruct the venous return and the parts bathed with permanganate solution Subsequently each tooth mark should be probed separately and cauterised or treated with pure phenol For 3 days the wound should not be sutured this particularly applies in the case of face bites

Antirabic vaccination—Owing to the long incubation period it is feasible to attempt immunising the patient either by the inoculation of attenuated living fixed virus, as in the Pasteur and Hogyes methods or by the injection of carbolised or etherised vaccines in which the fixed virus has been killed The Pasteur treatment consists of a series of 18 injections of emulsions made from the spinal cord of rabbits which had been dried for periods of from 14 to 3 days Semple introduced carbolised vaccine the most potent preparation consists of a 5 per cent carbolised suspension of sheep brain infected with Paris virus In mild cases the course consists of 2 ml. injected subcutaneously each day for 7 days in average cases of 5 ml for 14 days and in severe cases such as head neck and face bites in wolf bites, or in children bitten on the bare skin 10 ml are injected daily for 14 days Itchy swellings may appear at the site of the inoculations about the eleventh day but other complications following inoculation are fortunately rare. Paralytic accidents however have been recorded with all methods they include a mild facial neuritis dorso-lumbar myelitis and an ascending paralysis of Landry s type which is fatal in about 30 per cent of cases

Treatment of the paroxysm—No specific treatment is known Measures directed to alleviate the suffering of the patient should be instituted These include chloroform inhalations and morphine hyoscine chloral and atropine in large doses Curare has been employed for the relief of spasms

ACUTE ANTERIOR POLIOMYELITIS

Synonyms—Infantile Paralysis Heine Medin Disease

Definition—An acute infectious disease characterised in its fully developed form by local or widespread muscular paralysis consequent upon the destruction by the action of a specific neurotropic virus of anterior horn cells in the spinal cord or corresponding cells in the medulla

Ætiology—The disease occurs in both sporadic and epidemic manner and has its greatest incidence in countries in the temperate zones The most severe epidemics have occurred in the countries of northern Europe and North America but in the last 25 years it has appeared with increasing frequency in Australia New Zealand and South Africa and such island communities as Malta and Mauritius have not been spared During the War of 1939–1945 a particularly virulent form was prevalent in North Africa and the whole Mediterranean littoral

It shows a marked seasonal variation being commonest in the hotter months of the year In northern Europe the incidence usually begins to increase towards epidemic proportions in July and slackens off in October or November Sporadic cases however occur throughout the year

A conspicuous feature of the disease is its preference for the young although no age is immune In the early years of this century its maximal incidence among infants led to its being named infantile paralysis and at that time the greatest number of cases occurred in the second and third years of life Before the age of 1 year the infant appears to be immune

Over a period of 50 years there has been a steady tendency for the disease to attack older age groups and at present the maximal incidence is between the ages

is clear the patient remaining quietly at rest in bed Examination of the central nervous system reveals as a rule, nothing more than increased deep reflexes Glycosuria is not uncommon and vomiting exhaustion and emaciation characterise the final stage of the illness Death during the paroxysm may occur from dilatation of the right heart though sometimes near the end the spasms ameliorate or cease altogether

3 *Stage of paralysis* —If the patient survives long enough paralysis of various types including ascending spinal paralysis paraplegia and hemiplegia may supervene The patient lies helpless and exhausted and generally dies in coma In man this stage is rarely seen in canine transmitted rabies but paralytic rabies is commonly encountered in the bat transmitted variety in Trinidad

In the Trinidad outbreak all the cases were of this variety and all proved fatal The onset is acute with fever and headache Numbness and burning sensations in one or both legs paresis of the legs and retention of urine follow After 2 or 3 days the paraplegia becomes more complete and the plantar and tendon reflexes disappear One limb is commonly affected before the other In a few days the paralysis begins to ascend involving the muscles of respiration articulation and deglutition There is dyspnœa and restlessness The sufferer remains conscious but may be delirious Sensory changes are of variable intensity A final brief coma precedes the fatal issue During this time the temperature swings round 103° F and there is profuse sweating Hydrophobic symptoms are exceptional, and when present slight The cerebrospinal fluid yields an increased globulin content but is otherwise normal The duration of the illness is from 4 to 8 days

Rabies in the dog —These animals never show the hydrophobic syndrome observed in man The earliest manifestation appears to be a change in temperament followed by irritation and exacerbations of vicious fury in which the animal runs amok biting wildly anything in its path Later swallowing becomes difficult the bark is altered the jaw drops and general paralysis ensues Death invariably follows some 2 to 5 days after the first symptoms appear In dumb rabies the stage of excitation is absent.

Diagnosis —As a rule little difficulty is experienced in diagnosis but occasionally tetanus the cerebral type of typhus fever, bulbar paralysis from any cause and datura and other poisonings encountered in Oriental countries may need differentiation Lyssophobia or hysteroid counterfeiting of the disease generally manifests itself within the first 10 days and is unaccompanied by fever or other serious features

Prognosis —By no means all patients bitten by rabid animals die but once clinical manifestations appear the disease invariably ends fatally Estimates varying from 5 to 33 per cent have been made of the death rate in untreated patients but of those receiving early anti rabic inoculations in Pasteur institutes not more than 1 per cent die The mortality varies with the site of the bite the interposition of clothing the number of tooth marks the extent of tissue laceration and the rapidity with which efficient local treatment has been instituted Head face and neck bites are particularly dangerous as well as bites from wolves and jackals

Treatment —This is entirely preventive and in England the muzzling order and the strict quarantine of all imported dogs has led to the eradication of rabies In endemic areas canine bites should be promptly treated and the suspected dog chained up muzzled and kept under observation Should the animal be alive at the end of 10 days it is proof that the bitten person has not been infected This rule universally followed in Pasteur institutes is based (1) on the knowledge that the infected dog never survives longer than 6 days from the onset of its illness, and (2) that the saliva of a rabid dog is never infective for more than 4 days before the onset of symptoms In suspicious cases especially the head face and neck bites treatment should be commenced without delay and discontinued if the dog survives

The virus of rabies differs from that of yellow fever in not passing through the intact skin and where there is a history of being licked by an animal suspected of

rabies prophylactic inoculation need not be advised unless fresh skin abrasions were present at the time

Local treatment —If seen within 30 minutes bleeding should be encouraged by the application of a ligature just tight enough to obstruct the venous return and the parts bathed with permanganate solution Subsequently, each tooth mark should be probed separately and cauterised or treated with pure phenol For 3 days the wound should not be sutured this particularly applies in the case of face bites

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Over a period of 50 years there has been a steady tendency for the disease to attack older age groups and at present the maximal incidence is between the ages

of 5 and 10 This curious change in age distribution taken with the unfortunate fact that the incidence of paralytic poliomyelitis seems to increase rather than to decrease with the improved standards of hygiene in more advanced communities suggests that whereas in primitive communities children come frequently in contact with the virus in early life and so acquire immunity, those in more advanced communities escape this early inoculation, some of them only to fall victims to a virulent attack in later childhood

The successful transmission of the disease from man to monkeys by Landsteiner and Popper in 1909 and the subsequent researches of Flexner and Lewis and others as to the nature of the infecting agent proved to be landmarks in the development of our knowledge of virus diseases in general and of those of the nervous system in particular

It is now known that the causative agent of the disease is a virus which is amongst the smallest so far identified It is distributed widely in the human race and is commonly a harmless inhabitant of the naso pharynx and intestinal canal By modern methods it can be recovered from the naso pharyngeal washings and the fæces of both clinical cases and many contacts as well as from flies and communal sewage in affected areas It is now recognised that only a minority of the individuals harbouring the virus develop even mild symptoms of disease and that of these not more than a fifth develop paralysis There is thus a large pool of unaffected " carriers in any community that is affected and these probably play a major rôle in transmission of the disease This is in accordance with the known fact that 50 to 80 per cent of town dwellers in countries much affected by the disease have protective antibodies in their sera at a high titre Three distinct types of the virus have now been identified Type I (Brunhilda) which is at present the most virulent and carries the highest incidence of paralysis Type II (Lansing) which can be adapted to be pathogenic to rodents and Type III (Leon) All three types have been responsible for paralytic attacks in the human They are serologically distinct but it is at present by no means clear to what extent infection with one type confers protection against the natural disease caused by the other types The rare occurrence of second attacks of the disease strongly confirms that cross immunity is incomplete

A clinically recognisable attack of poliomyelitis whether paralytic or not leads to the development of specific antibodies in the blood which with the rare exceptions mentioned above confer lifelong immunity from a further attack Such antibodies are not present in the sera of individuals from isolated and unaffected communities or in those of susceptible individuals in affected communities On the other hand the high incidence of natural immunity among adults especially the town dwellers in affected populations confirms the belief that one or more subclinical attacks occur during many such persons lifetimes The immune body is carried by the gamma globulin fraction of the plasma and is at present the subject of intensive research in the hope of finding a satisfactory method of immunisation against the disease

The method of spread of the infection has been a matter of controversy for many years It has been generally accepted that unaffected carriers play a larger part in the process than do recognisable cases of the disease Although the participation of flies in the spread of the disease cannot be excluded it is clear that the principal agency concerned is human contact The main matter of dispute has been whether the infection is carried by droplet spread from the naso pharynx and upper respiratory tract or by the various methods of fæcal contamination from the gastro intestinal canal The evidence for droplet spread is strong and epidemiological studies have shown a close association between cases of the disease and human movement in circumstances in which spread by the excreta was unlikely The undoubted association between tonsillectomy and the development of bulbar poliomyelitis also indicates the naso-pharynx as a potential source of infection On the other hand the major incidence of the disease in hot weather has always suggested that it was spread by

fæcal contamination and there is now convincing evidence that the gastro intestinal tract acts as a portal of entry for the virus and that in most epidemics it is the principal one The virus can be recovered from the stools of patients for several weeks after an attack as well as from those of intimate contacts and from communal sewage The method of transmission is largely by human contact operating through such agencies as contaminated food eating utensils and latrines It is possible that milk and water may also play a part Although the virus can be recovered from flies in infected areas the part they play as vectors has not yet been determined It used to be said that case to case infection did not occur, but this statement will no longer bear critical examination However such occurrences are extremely rare in institutions where cases are treated with careful barrier nursing precautions

There is still considerable uncertainty as to how the virus when it reaches a susceptible host in adequate dosage breaches the defences of the body surface and reaches the nervous system There is evidence that in so doing it is aided by a lowering of the victim s general resistance or by local trauma such as tonsillectomy or by local disturbance such as may cause the diarrhœa which often precedes attacks in which a gastro intestinal origin of the infection is to be suspected Since the work of Hurst and Fairbrother later confirmed by Howe and Bodian it is evident that the virus having penetrated the body s defences reaches the nervous system by axonal pathways The original view that the olfactory nerves were the agents of transmission has been abandoned and it is now thought that the nerve fibres of the gastro intestinal canal and of the tonsils are responsible The virus is capable of transmission along axones but can only proliferate in the bodies of nerve cells Examination of the nervous systems of humans or of experimental animals dying of the disease shows that the virus is widely distributed in the brain and spinal cord but reaches its highest concentration in the anterior horn cells of the spinal cord especially of the lumbar enlargement the motor nuclei of the brain stem and motor cells of the cerebral cortex Another subject of controversy has been whether the entire sequence of events observed in acute poliomyelitis can be explained in terms of a process confined to the nerve cells or whether there is an associated systemic infection The high proportion of cases in which no paralysis occurs the associated blood changes and the widespread occurrence of immune bodies in the blood stream are points suggestive that a systemic invasion does take place although the virus has only rarely been recovered from the blood in human cases and the visible pathological changes seen after death are confined to the nervous system An interesting association has been shown to exist between intramuscular injections such as may be given for purposes of immunisation and the development of paralysis in neighbouring muscles during succeeding weeks This is now believed to be due to the action of poliomyelitis virus determined by the specific local trauma of the injection

Pathology —The virus of poliomyelitis is an obligatory intracellular parasite and its action takes place entirely within the nerve cell The changes seen in the nervous system vary with the virulence of the infection The virus has a special affinity for the anterior horn cells of the spinal cord and in severe infections these cells in portions of the cord undergo acute necrosis If the experimentally infected animal be destroyed at this initial stage no lesions other than these cell changes are found and the rapidly ensuing cellular exudation and meningeal infiltration seen in fatal human cases are not present But the necrosis of nerve cells in the surviving patient is naturally soon followed by phagocytic processes and amœboid (microglial) cells and polymorphonuclear leucocytes rapidly invade the affected areas and clear away the dead nerve cells It is essential to bear in mind however that these processes are secondary and not as used to be thought the primary and essential lesion of poliomyelitis In less severe infections less acute forms of nerve cells changes are seen and with these the cellular exudation is almost wholly of amœboid microglia cells These phagocytic cells fill the perivascular spaces in the affected parts of the cord Together with

leucocytes these cells finally overflow into the cerebrospinal fluid They may appear here even before the development of paralysis and it was this early indication of meningeal infiltration that led to the view formerly held that a meningitis preceded the involvement of the nervous system In the affected regions of the grey matter of the ventral horns some cells always remain unaffected by the virus Some degree of encephalitis is a constant feature although it is not usually clinically manifest

Lesions in the viscera have been described namely, hyperplasia of the lymphoid tissue and splenic enlargement—but these are not constant and their presence at the final stage of the malady is of uncertain significance

Cerebrospinal fluid—The fluid is clear colourless or faintly yellow and under normal or only slightly increased pressure and the titre of chlorides and sugar is normal The protein content is slightly increased at first and tends to rise during the first 3 weeks after the onset of the disease The cell content of the fluid is very variable In the majority of cases there is a pleocytosis of 20 to 100 cells per c mm but there may be more The count is usually a mixed one with lymphocytes outnumbering the polymorphs in a proportion of two or three to one In some cases however a high proportion of polymorphs may be found at the onset usually giving place to a predominantly lymphocytic increase in subsequent punctures The fluid may be normal in indubitable cases The nature and number of the cells seem not to afford any prognostic indications

Blood—In the early stages of the malady there is usually a polymorphonuclear leucocytosis which may reach as high as 30 000 This leucocytosis disappears when the fever abates

Symptoms—It is now generally believed that infection with poliomyelitis virus is a much commoner event than was formerly supposed and that of those so affected only a relatively small proportion develop symptoms of a kind sufficiently definite to permit of a clinical diagnosis Of these latter probably not more than a fifth are destined to develop paralysis This has led to the recognition of three degrees of poliomyelitis viz (*a*) formes frustes abortive cases or the minor illness (*b*) pre paralytic and non paralytic poliomyelitis (*c*) paralytic poliomyelitis This clinical subdivision is justifiable and useful on practical grounds but it should be understood that there is no corresponding pathological subdivision and that the three degrees shade off imperceptibly into one another

(*a*) *Formes frustes or the minor illness*—Such cases occur sporadically and are particularly plentiful in times of epidemics They can rarely be diagnosed with certainty although their nature may be suspected in the presence of an epidemic or retrospectively when other cases have occurred in the same family or isolated community The symptoms consist of malaise headache mild fever aching in the back and limbs and sometimes a sore throat or mild gastro intestinal upset and are thus common to influenza the pre eruptive stages of the exanthemata and such virus diseases as infective hepatitis or glandular fever The disturbance subsides in 24 to 48 hours without residual symptoms and the spinal fluid if examined is usually normal

(*b*) *Non paralytic and pre paralytic poliomyelitis*—The symptoms are essentially the same as in the minor illness but rather more intense and prolonged The onset is often abrupt and fever practically invariable The temperature is commonly 103° or 104° F and this pyrexia commonly lasts for 2 to 4 days and then gradually subsides sometimes finally and sometimes to rise again a few days later and before the paralysis makes its appearance Pains in the back and limbs are more severe and flexion of the spine is painful Vomiting and anorexia are common and in many cases there is slight diarrhœa After a day or so the general headache becomes intensified and occipital in position and is associated with the classical symptoms of meningeal irritation namely irritability neck stiffness and photophobia The muscles of the back and limbs are often tender and may show tremor and depression or loss of their reflexes There may be retention of urine

Such a clinical picture in an adolescent or young adult in the summer or early autumn is extremely suggestive of poliomyelitis but to those who have had extensive experience of epidemics the picture seen in young children is highly characteristic Draper has given a vivid account of this stage from which the following account is taken The child is commonly flushed and miserable and may be drowsy, but it presents a typical appearance of mingled apprehension and restlessness and may be very irritable In severe infections the child breathes rapidly appears preoccupied and in a state of tenseness An ataxic tremor and involuntary muscular jerkings may be present. Extreme fearfulness and confused and alarming dreams are common The child is hypersensitive to even the lightest touch and resents being moved Vomiting probably of central origin may also be present Headache pain in the neck and back stiffness of the spine and pain in the back on active or passive flexion, diminution of tendon jerks and some diffuse weakness all appear in sequence

During this stage of the illness it is impossible to predict with certainty whether the symptoms will gradually subside or whether paralysis will suddenly declare itself and if the nature of the disease has been recognised an agonising period of waiting is inevitable and may be prolonged for 2 or 3 days

Generally speaking severe fever and meningeal signs and depression of tendon reflexes are of grave significance but mild premonitory signs may be followed by severe local or general muscular paralysis It should be remembered that probably not more than one fifth of the cases diagnosed and in many cases confirmed by C S F changes subsequently develop paralysis

(c) *Paralytic poliomyelitis* —In these cases usually at the height of the constitutional and meningeal disturbance muscular paralysis declares itself It may be confined to the muscles innervated by the spinal cord—the spinal form—or affect those innervated by the bulbar nuclei either exclusively or in addition to spinal paralysis—the so called bulbar poliomyelitis or polio encephalitis

1 SPINAL FORM —The onset of paralysis occurs usually between the second and the fifth days of the constitutional disturbance but may be delayed as long as the tenth day if the fever persists From the moment of its first appearance it usually reaches its height within 24 hours but in rare cases it may continue to become more severe for several days or recrudesce after becoming stationary

In distribution and severity the paralysis varies over the widest possible extent At one end of the scale are those cases in which within a few hours all four limbs are completely paralysed and the patient is engaged in a life and death struggle with respiratory failure At the other are cases so mild that the paralysis is not recognised till the patient starts to get up Generally speaking the legs and lower trunk muscles suffer more frequently and severely than the upper parts of the body especially when diarrhœa has been a feature of the invasive period

Wherever it occurs the paralysis is of the flaccid lower motor neurone type with loss of muscle tone loss of voluntary power varying from weakness to complete paralysis and diminution or loss of the corresponding tendon reflexes This is rapidly followed by wasting which in severe cases is rapid and intense in degree Until it has been seen the rate at which the muscles dissolve under one s eyes can hardly be believed Such muscles are frequently tender and sometimes show spasm so that the development of contractures occurs both easily and rapidly The paralysis is generally much more widespread and severe at its commencement than it is destined to be permanently At first all four limbs may be completely helpless and later there may be complete recovery in all but one limb The widely spread temporary paralysis is due to a recoverable affection of nerve cells whereas the permanent paralysis is the result of actual destruction of nerve cells by the necrotic lesion Usually the muscles first affected are the ones that show the greatest permanent damage

In the rare ascending type the paralysis may gradually ascend from the legs and lower trunk to the upper limbs and progressive deterioration of the respiratory

muscles during the first day or two after the onset of paralysis is relatively common and is probably due to progressive exhaustion of the nerve cells of the upper thoracic and cervical region themselves a little damaged by the failure of the lower thoracic muscles to carry their share of the respiratory burden In cases where the cervical cord is involved respiratory embarrassment makes its appearance early and in the absence of artificial respiration in some form it may lead to a fatal outcome within a few hours of the onset of paralysis

In cases which survive the narrowing down of the initial paralysis begins to show itself after the end of the first week and any muscle which will recover useful power will have done so before the end of the third month The paralysed muscles undergo atrophy which is more rapid and complete in those cases in which there will be no subsequent recovery they give the reaction of degeneration They are flaccid from the first and in the course of time tend to develop a variable degree of contracture and yet it is common to see a limb which remains permanently flail like Any muscle which shows a response to faradism 3 weeks after the onset will usually recover completely When a limb is paralysed there is usually a considerable degree of vasomotor paralysis, and there may be subsequent retardation of growth Considerable deformities of the body and limbs may arise as the result of the loss of support which results from the paralysis from the action of unopposed muscles and from the contractures Such deformity may involve actual dislocation of joints as in the shoulder joint when the deltoid is paralysed and the pectorals escape

The local lesion of the spinal cord is by no means confined to the grey matter and may occasionally involve the contiguous white matter of the lateral column sufficiently to give rise to signs of lesion of the pyramidal tract and in rare cases of lesion of other neighbouring tracts such as the spino thalamic tract, with a result in a Brown Séquard s syndrome of pyramidal deficiency upon the same side and loss of pain and temperature sense on the opposite side below the lesion This is the so called ' myelitic form Paralysis of the cervical sympathetic is occasionally seen when the lower part of the cervical enlargement is involved with the usual signs of a small pupil and low lying lid on the affected side It is however, generally a transient event

Disturbances of sensibility of an objective kind are rare and are almost always transient, and amount to blunting of pain and temperature sensibility from involvement of the spino thalamic tracts which are contiguous to the ventral horns Subjective disturbances are common and consist of severe local pains in the limbs, back and neck Tenderness of the muscles and pain on moving the joints are sometimes very prominent and may persist for many weeks The dominance of the clinical picture by persistent pains in the periphery constitutes the so called neuritic' form of poliomyelitis

The reflexes both superficial and deep are at first lost in the affected region and indeed are generally absent throughout the body in the early stages of a severe case, from the general effect of the virus upon the nerve elements In the later stages they return or remain permanently absent according as the muscles recover or not The preservation of a tendon jerk or any sign of a returning reflex either deep or superficial in the early days of the illness is a most useful prognostic indication that the muscles concerned with the reflex will entirely recover

Retention of urine is common during the first 10 days of the illness particularly in the case of male subjects where the trunk muscles are involved It is never permanent

2 Brain stem Form or Bulbar Poliomyelitis —Involvement of the muscles innervated by the bulbar nuclei may be present from the onset and may be encountered in the absence of spinal cord symptoms This is commonly seen in the cases occurring as a complication of tonsillectomy More often however it occurs as an extension of the disease in cases in which the cervical enlargement of the spinal cord is involved and respiratory complications are already present Its onset is often

heralded by mental confusion and drowsiness acceleration and irregularity of the pulse irregularity of the respiratory effort and flushing and congestion of the skin and conjunctivæ These symptoms may be confused with those of anoxia Excessive bronchial secretion occurs and adds to the danger of this grave complication Paralysis of the pharynx may be unilateral or bilateral and leads to dysphagia and to the accumulation of secretions in the pharyngeal recesses Laryngeal paralysis may be partial or complete and may lead to dangerous adductor spasm Paralysis of the tongue may occur The palate is commonly involved giving rise to a nasal speech and regurgitation of fluids down the nose Unilateral or bilateral facial palsy is common but similar paralysis of the muscles of mastication is much more rare but occasionally the patient may be unable to keep the jaw shut Ocular paralyses are very rare and patients showing them are usually moribund Occasionally however spontaneous nystagmus occurring in short bursts and at a rapid rhythm may be seen and is not of particularly sinister significance

The occurrence of bulbar symptoms is always an event of grave prognostic significance but if the patient survives the cranial nerve paralyses make a remarkably complete recovery

Diagnosis —When once paralysis is present the diagnosis of poliomyelitis seldom presents much difficulty In children a localised paralysis has to be distinguished from such causes of ' *pseudo paralysis as acute rheumatism osteomyelitis syphilitic* epiphysitis and scurvy with subperiosteal hæmorrhage In all these there may be associated fever and general disturbance with pain and reluctance to move the limb

In cases of generalised paralysis the group of diseases most likely to be confused with poliomyelitis are the peripheral neuritides particularly acute infective polyneuritis and acute porphyria In both of these the paralysis is symmetrical and at first peripheral in distribution and although slight some sensory disturbances are usually present The finding of a C S F with a high protein content but no excess of cells is a point in favour of polyneuritis Cases of poliomyelitis affecting both legs and the lower part of the trunk may easily be confused with acute compression of the spinal cord in the dorsal region with a flaccid paraplegia especially when this is caused by an infective lesion of the spine such as osteomyelitis Careful attention to the history and the finding of sensory loss with a clear upper level will usually suffice to avoid this mistake

Isolated bulbar poliomyelitis may be confused with focal lesions of the medulla such as syringobulbia or vascular lesions and a very similar picture may be seen in botulism

It is particularly in abortive cases and in the pre paralytic stage that difficulty in diagnosis arises Indeed it is often impossible to diagnose poliomyelitis with certainty though it may be suspected in the presence of an epidemic or on account of the time of year

In cases showing merely fever malaise and some generalised muscular pains the differential diagnosis is from influenza tonsillitis and the exanthems These are rare in summer and early autumn More difficult to distinguish are the premonitory phases of certain other virus diseases namely infective hepatitis glandular fever and *virus pneumonia*

When signs of meningeal irritation are prominent the diagnosis is from the various forms of meningitis though it should be borne in mind that all the conditions mentioned above may be associated with meningism

The pyogenic meningitides usually present a picture so definite that serious difficulty does not arise but meningococcal meningitis may start insidiously and tuberculous meningitis relatively acutely The distinction from these conditions can usually be made with certainty on the cerebrospinal fluid but this may take a day or two

Greater difficulty occurs with benign lymphocytic meningitis and with the meningo encephalitis of mumps which may precede the parotitis as in both cases a pleocystosis

similar to that of poliomyelitis occurs with no fall in glucose, or chlorides and little increase in protein

The meningeal reaction to a cerebral or extradural abscess may also give a mixed pleocytosis with a sterile fluid but here there is usually a considerable increase in the total protein content

Course and Prognosis—A good deal has already been said on these aspects of poliomyelitis in the foregoing paragraphs In abortive cases and non paralytic cases which represent the vast majority of the total, recovery is complete though patients will often notice general lassitude and even a marked loss of weight for some weeks or months after the illness

Purely local paralysis presents no threat to life and the patient recovers with a varying degree of local disability It is not uncommon to see cases of complete paralysis of all muscles below one knee or of one shoulder girdle and spinal deformities may later develop from involvement of portions of the spinal musculature

Cases of generalised paralysis are always in grave danger because of the likelihood of involvement of the respiratory musculature and this complication is the principal cause of death However if the emergency is surmounted remarkable recovery of respiratory function occurs In part this is due to the development of increased efficiency in the remaining respiratory muscles including the accessory muscles but partly to the fact that the initial loss of power in diaphragm and intercostals is often due to exhaustion rather than to irreparable anterior horn cell damage

In cases surviving the first impact of the disease improvement in muscle tenderness begins after a week or so and recovery of function of muscle begins about the same time It usually begins first in the muscles last affected and in cases destined to make a good recovery it continues at a rapid rate for 2 to 3 months Recovery of tendon reflexes or the faradic response often precede the return of voluntary power Muscles which show no sign of recovery and have the reactions of degeneration at the end of this time are unlikely to make any useful recovery After 3 months recovery continues at a gradually slower rate for another 6 months but most of the improvement during this period results from the development and adaptation of function in already active muscles rather than from further recovery of nerve cells

In all but very mild generalised cases some degree of permanent wasting and weakness of muscles will remain which may necessitate the use of various appliances to improve function and mobility and various orthopædic procedures to the same end In severe cases the patient may be left permanently confined to a spinal chair or wholly dependant for life upon some form of respirator and he is faced with all the problems of psychological readjustment that this implies

In young children and to a less extent in adolescents the loss of muscle may lead to serious defects of growth in the limbs and to deformities both of the limbs and the trunk

The occurrence of bulbar symptoms increases greatly the gravity of the prognosis but if the patient survives the cranial nerve palsies usually undergo complete recovery

Second attacks of poliomyelitis occur but are exceedingly rare They probably result from a susceptible individual encountering at different times strains of the virus which do not confer cross immunity

Treatment—The first problem that faces a physician called to see a case of poliomyelitis is disposal Should the patient be left at home or moved to a hospital and if the latter to what hospital ? In abortive and pre paralytic cases this decision is a difficult one If on balance the diagnosis seems likely to be poliomyelitis and particularly if the existing symptoms are severe the decision should be for immediate transfer as a respiratory emergency may arise suddenly at any time If the case is mild or the fever already subsiding it may be justifiable to leave the patient at home In that case absolute bed rest should be enjoined for there is satisfactory evidence that the taking of vigorous physical exercise in the pre paralytic stage may not only

greatly increase the likelihood of paralysis occurring but may also determine its distribution The child should remain in bed for 2 weeks after all fever and symptoms have subsided and get about gradually during the third week Contact with other children should be avoided for 3 weeks after the temperature becomes normal and for the same time the excreta should be immersed in lysol for 12 hours before disposal No restrictions need be placed on diet though at first the appetite is usually poor

If it is judged that the diagnosis is probable or beyond doubt—and this will include all paralytic cases in the acute stage—the case should be transferred to hospital and is notifiable The choice of hospitals may in this country at least present a difficult problem From the public health point of view admission to a fever hospital where facilities exist for complete isolation is the disposal of choice and is the accepted policy of the Public Health authorities From the patient s point of view this may also be satisfactory in large cities where sufficient cases occur to make it a practical proposition to assemble together the trained nursing staff the experienced medical officers and consultants and the wide range of instrumental equipment needed to deal with the many emergencies that may arise during the course of a case of poliomyelitis But in smaller centres and in the country fever hospitals are not so provided and are often unsuited to cope with acute cases of this disease The alternative to a fever hospital is a well equipped general hospital Here cases can be nursed either in isolation cubicles or with barrier precautions the standard of nursing is usually high and the full range of consultant and specialist assistance both for the acute and convalescent stages is available Under such circumstances transmission of the disease to nurses medical officers or other patients is exceedingly rare and in the view of most of those in a position to judge, a general hospital is to be preferred to all but the best fever hospitals for such cases

The ideal solution of the problem is the setting up of regional poliomyelitis centres where a specially trained staff both medical and nursing is immediately available and all instruments and equipment are kept permanently ready for use

Whatever the hospital in which the case of poliomyelitis is treated it constitutes a potential emergency of the most dramatic kind Treatment falls into three natural phases

(*a*) The acute illness lasting from the onset for 2 or at most 3 weeks
(*b*) The stage of neuronic recovery lasting for 6 months or so from the onset
(*c*) The stage of adaptation and rehabilitation lasting up to 3 years from the time of the acute illness

(*a*) *The acute illness* —Here the primary object of treatment is to ensure the patient s survival He should be nursed on a soft mattress or air bed upon a stiff wire bed or fracture boards All excreta linen and feeding utensils should be sterilised and kept separate from those of the other patients and all attendants should wear masks and gowns The diet should be light but as nutritious as the patient will tolerate

All muscles showing weakness or paralysis should be put as far as possible in the *position of physiological rest The feet and toes should* be supported at right angles to the legs by pillows and a vertical board The knees should be maintained at 10 flexion by a slender bolster underneath them If the deltoids are affected the shoulders should be kept abducted by pillows to as near as the patient will tolerate to 90 The hand should be dorsiflexed at the wrist to 30 with the fingers and thumbs gently flexed round a small woollen cushion Pain and spasm in muscles may be relieved by hot packs and the discomfort may necessitate the use of aspirin or other analgesic and even of morphine provided that this is not contraindicated on other grounds From the beginning all joints should be put through their full range of passive movement twice a day and the complete immobility formerly insisted upon is now regarded as harmful and responsible for much of the painful limitation of

movements at joints and muscular contractures which can be such a tiresome feature of the convalescent phase Retention of urine is best treated by an indwelling catheter and seldom lasts more than 2 weeks even in severe cases If cystitis develops it should be treated immediately by means of sulphonamides or the appropriate anti biotic and, if severe this should be combined with tidal drainage and bladder washouts

The complications of poliomyelitis which threaten life are respiratory failure and bulbar involvement.

Respiratory failure —Although this commonly develops suddenly during the first 2 or 3 days of paralysis it does not do so without warning Frequent and careful examination of the chest may reveal the progressive involvement of the intercostal muscles on one or both sides and may be confirmed by asking the patient to count aloud without drawing breath An initial count of 50 or more may fall to 20 before the patient is conscious of dyspnœa at rest Spirometer readings should be taken at regular intervals and starting at 3000 to 4000 ml may fall on successive measure ments to 1200 ml or so before cyanosis is visible or subjective distress is experi enced

It is often the involvement of the diaphragm which precipitates a respiratory crisis and necessitates the use of some sort of artificial respirator If the emergency develops suddenly as it often does within 12 hours of the onset of paralysis the decision to use the respirator presents no difficulty If it develops gradually over several days from progressive exhaustion of the remaining respiratory muscles a difficult choice has to be made There is a natural reluctance to submit a sick person to the terrifying experience of dependance for life upon a machine but it should be remembered that this experience is much less of an ordeal if it occurs before it is obligatory Further more, throughout the period of gradual respiratory failure the lungs are undergoing a process of lobular collapse and if atelectasis occurs it takes some days to re expand the collapsed areas even with adequate respiration Generally speaking therefore it is preferable to resort to a respirator too early rather than too late and a rapidly falling respiratory exchange as indicated by a vital capacity of less than 1500 ml in an adult is an indication for the use of a respirator

The effects of respiratory embarrassment are often aggravated by the accumula tion of bronchial secretions frequently excessive in amount which the patient is unable to cough up This complication can often be forestalled especially in children, by postural drainage The patient is laid face downwards on a thoracic bed with the head and chest sloping downwards at 30 to 45° In other cases it may be necessary initially to suck out the secretions through a bronchoscope

A number of artificial respirators are available for choice That of most general application is the Drinker respirator and its various modifications in which the entire patient except for his head is enclosed in an airtight tank The air in this is rhythmic ally sucked out by bellows operated by an electro motor in such a way that the negative pressure so created draws air into the patient s thorax A sorbo rubber collar secures an airtight fit round the neck and portholes are provided for nursing and inspection The whole floor of the tank carrying the patient can be drawn out for more prolonged attention

The tank respirator gives satisfactory results when properly employed but certain risks are associated with its use Secretions in the trachea and bronchi are liable to be drawn into the alveoli ventilation can be too deep or too rapid with consequent disturbance of the blood chemistry or it may be insufficient and so give rise to pro gressive anoxia The motor may break down and an efficient engineer is as much a part of the team in a respirator unit as efficient nurses and doctors The patient s colour pulse and subjective sensations are a better guide to the efficiency of respiration than blood gas analyses

Of other respiratory aids available some operate by negative and some by positive

pressure Various cuirass respirators which may be useful for transport act by suction but enclose the thorax only The Bragg Paul respirator consists of a distensible jacket which encloses the chest and rhythmically expresses the air from the chest relying as does manual artificial respiration upon the elasticity of the chest wall to re expand the lungs

Recently positive pressure machines operating with a face mask such as is used in closed circuit anæsthesia have been introduced and are particularly useful in combination with the Drinker respirator for enabling the patient to remain out of the tank long enough for nursing care and physiotherapy Whatever type of respirator is used the personalities and training of the attendants are of paramount importance and every effort should be made to avoid frequent changes in personnel

Bulbar poliomyelitis —When this occurs in the absence of respiratory involvement or of widespread mesencephalitis it is a relatively benign condition Dysphagia may necessitate feeding by nasal catheter and the accumulation of secretions in the nasopharynx and upper respiratory passages may necessitate postural drainage or repeated suction The occurrence of adductor spasm of the vocal cords may require tracheo tomy Recovery is the rule Bulbar poliomyelitis with mesencephalitis and signs of more generalised polioencephalitis is usually a terminal event in a moribund patient

It is when it occurs—as it usually does—as a complication on the second or third day of a case of spinal poliomyelitis of the cervical and thoracic cord with respiratory involvement that bulbar poliomyelitis presents a therapeutic problem of the greatest difficulty It is associated with excessive bronchial secretion and often with laryngeal obstruction which with a patient already in a respirator has usually led to rapid death In a recent epidemic in Denmark where such cases were common the mortality was nearly 90 per cent until the drastic measure of immediate tracheotomy and positive insufflation followed by regular suction was adopted This procedure reduced the mortality to approximately 25 per cent but the method makes the greatest possible demands upon medical and nursing attendance and is clearly only possible in specially developed centres With the modern methods outlined above it is not uncommon for a patient to survive the immediate emergency only to become permanently de pendant upon artificial respiration—a dilemma of a most poignant kind for all concerned

(*b*) *The stage of neuronic recovery* —During this period which lasts for 3 to 6 months in severe cases the objects of treatment are to promote the maximal recovery of nerve cells and therefore of muscles to restore function and to prevent contractures and deformities The patient is best treated in a specialised convalescent unit such as is often associated with orthopædic centres Massage and passive movement of limbs should gradually give way to active movements carried out at first with slings or in warm baths and later against progressively increasing resistance Weight bearing should be assisted by such devices as bannisters crutches and calipers Such devices as stationary bicycles and boats and the intelligent use of ball games play an important part and progress is more rapid in cheerful and well run units where group methods are possible and the elements of competition and emulation can be made use of

Care must be taken to prevent the development of deformities and where the trunk muscles are involved the patient should spend several hours a day lying prone on a flat bed to correct the tendency to develop a lower thoracic and lumbar kyphosis Breathing exercises should be given

After 6 months it is unlikely that more neurones will recover their function and improvement becomes much slower It continues however for many months or even years by virtue of the increased adaptation of the patient to his disability and by the hypertrophy and taking over of new function by existing muscles

(*c*) *The stage of adaptation and rehabilitation* —This is really a continuation of the

above and may last 2 to 3 years In it function gradually improves and the patient's range of activity increases Instrumental devices may be used and in many cases the patient has to be trained for a new occupation depending upon the nature of the residual paralysis and the natural aptitudes of the individual After 2 years operative orthopædic procedures may be needed to stabilise flail joints or to improve function by tendon transplants

Specific Treatment —The virus of poliomyelitis is not susceptible to any of the existing antibiotics or other known drugs As early as 1910 Netter tried to minimise the extent or severity of the paralysis by injecting convalescent human serum but without success In spite of claims to the contrary, all subsequent attempts to affect the acute illness by antisera have proved useless This is in conformity with what occurs in other virus diseases of the nervous system and it has been shown that in experimental poliomyelitis in order to prevent the development of the disease after the injection of virus into the nervous system the immune serum must be injected within 12 hours of the injection of the virus

PROPHYLAXIS —In view of the generally accepted observation that tonsillectomy may precipitate bulbar poliomyelitis this operation should not be carried out during epidemics of the disease Similarly injections of immune sera or inoculations against diphtheria should be avoided Much progress has been made in recent years in the field of immunisation against poliomyelitis Passive immunisation by means of serum or gamma globulin can play at best only a limited part in the prevention of the disease Active immunisation with killed virus on the other hand offers better hopes of protection and has been used extensively in the United States and other countries The Salk formalin inactivated polyvalent vaccine received an initial set back in 1955 when over 200 cases of poliomyelitis in the United States were attributed to its use but stricter safety standards for its manufacture and testing have since been imposed and millions of children have been inoculated without mishap Active immunisation has also been achieved by giving suspensions of live attenuated virus by mouth to human volunteers Virulent strains can be rendered avirulent by frequent passage through mice or cotton rat brain while retaining their antigenic quality The results however although encouraging are still *sub judice*

PRECAUTIONS IN SCHOOLS —A common problem arises when a case of poliomyelitis occurs in a boarding school and medical advice is sought by the school authorities or the children s parents It should be borne in mind that at present medical knowledge is insufficient to give an entirely satisfactory ruling in the matter We do not know exactly how long an individual continues to pass virus in his excreta or droplets nor do we know fully how the infection is spread or how the virulence of the virus and the susceptibility of individuals may be measured Furthermore such is the fear of the disease in the public mind that parents cannot be expected to behave entirely rationally with regard to it

If more than one case occurs in a school the best course is to put the school as a whole in isolation All intercourse with other schools should be cancelled the pupils should be confined within bounds vigorous games and swimming should be suspended and any child developing mild symptoms should at once be confined to bed in the sanatorium Ideally the school should not be dispersed as it is likely that the majority of the pupils have already come in contact with the source of infection and may themselves be a source of danger to others The arbitrary period of 3 weeks is usually accepted for isolation Unfortunately the majority of parents will insist upon removing their children and this cannot be prevented Parents should be advised to notify their own practitioner immediately on the child s return home and he should be kept away from other children and from such places as swimming pools cinemas etc for 3 weeks Again, strict bed rest should be enforced if any mild febrile disturbance should show itself

VASCULAR DISORDERS OF THE NERVOUS SYSTEM

ARTERIAL THROMBOSIS AND HÆMORRHAGE

Cerebral thrombosis and cerebral hæmorrhage seem hitherto to have been described in textbooks of medicine as quite separate conditions almost antagonistic and mutually incompatible between which it was possible and even highly essential to make a differential diagnosis for the purpose of applying very dissimilar lines of treatment in the respective conditions each line of treatment being the worst possible for the other condition It cannot however, be too forcibly pointed out that primary arterial thrombosis and primary arterial hæmorrhage depend in every case upon degeneration of the arterial wall and that every condition of degeneration of the arterial wall may cause either thrombosis or hæmorrhage indifferently It is a usual experience to find in patients who have had several strokes that thrombosis was the cause of the earlier and hæmorrhage of the final apoplexy Even in that condition which has always been held to be the most important antecedent of cerebral hæmorrhage—renal disease with high arterial tension—thrombosis and not hæmorrhage is the cause of apoplexy in many cases On account therefore of the identity of the underlying pathological condition in every case and the clinical association of thrombosis and hæmorrhage of the cerebral arteries and the difficulty of distinguishing them clinically the two conditions are here described together

Ætiology and Pathology —The arterial degeneration which may result in cerebral thrombosis and hæmorrhage is due to the following causes (1) Arteriosclerosis which is the common cause both of thrombosis and of hæmorrhage in the second half of adult life and which is by far the most frequent cause of hæmorrhage It must be especially borne in mind that cerebral atheroma may be local in the cerebral vessels and unassociated with general atheroma of the systemic vessels (2) Syphilis which was formerly the commonest cause of thrombosis in the first half of adult life and which is less frequently the cause of hæmorrhage It may affect both the large and the small arteries even to the smallest All the coats of the artery are affected and in the finest vessels there is conspicuous lymphocyte accumulation or cuffing round the vessel (3) Periarteritis nodosa Buerger s disease and other less common varieties of arterial disease (4) Abnormal conditions of the blood especially when associated with heart failure as in septicæmic conditions Hæmorrhage into the brain may also complicate polycythæmia and acute leukæmia (5) In association with new growths of the brain both thrombosis and hæmorrhage are common events especially when the neoplasm is soft and rapidly growing The vascular lesion may occur quite early in the course of the new growth and apoplexy may be the first sign of its presence (6) Inflammatory conditions of any nature may cause thrombosis and hæmorrhage The vascular lesions are usually small but they may be extensive and may cause death (7) Traumatic lesions such as the passage of a bullet through the brain or a blow upon the head or concussion from high explosives may cause extensive thrombosis or hæmorrhage (8) Cerebral hæmorrhage results often enough from the direct rupture of a true aneurysm or angioma or of one of those irregular local thinnings of the vessel wall which is called a false aneurysm and may take place from an artery the wall of which is softened by disease though there be neither thinning nor bulging of the vessel wall

Syphilitic cerebral thrombosis is not usually a pure pathological process for the vascular disease is often accompanied by acute syphilitic encephalitis with much lymphocyte extravasation in the vicinity of the diseased vessels and acute local œdema which increase the ischæmia when thrombosis occurs The symptoms of loss of

cerebral function are not all due to the thrombosis but are *in part due to the recoverable* acute inflammatory condition and it is for this reason that syphilitic apoplexy often shows much more recovery than do other varieties

Thrombosis is a more common cause of apoplexy than is hæmorrhage but it is much *more frequently survived while hæmorrhage is frequently fatal* within from a few hours to a few days of its onset It follows therefore that in the necropsy room of a general hospital hæmorrhage *is seen much more often than is thrombosis* while in infirmaries where the survived cases of apoplexy collect, thrombosis is almost *invariably the lesion found to be responsible* for the apoplexy

Thrombosis tends to occur when an habitually high blood pressure is temporarily lowered and the circulation less active, and is always strongly suggested when apoplexy occurs during sleep and conditions of quiet, and after exhaustion exposure to cold severe purgation and in debilitated states generally It is preceded by slowing of the circulation in the area affected and this may be productive of prodromal symptoms Or there may be slight local thromboses preceding the main thrombosis also giving rise to prodromal symptoms Thrombosis may thus have an ingravescent onset especially when clotting occurs in distal branches of an artery and extends towards the main vessel, but on the other hand it may have an absolutely sudden onset when the clotting occurs primarily in a large artery The immediate effect of the thrombosis is a condition of infarction with œdema extending widely in the vicinity and it is this œdema which causes the loss of consciousness so commonly seen a few hours after the apoplexy has occurred The œdema tends to pass off in a few days and the area bereft of circulation by the thrombosis tends to become narrowed by collateral circulation from surrounding regions and any recovery of function within the affected region must be by collateral circulation from elsewhere In many cases however—perhaps the *majority* of those which are clinically ascribed to cerebral thrombosis—actual thrombosis does not occur but cerebral tissue to which the circulation has been inadequate *for a long time eventually undergoes* softening rather abruptly There is little essential difference between the two groups of cases and it *is customary to apply the term* cerebral thrombosis *to all* *The affected* area at an early stage is bright red in colour and soon becomes soft and shrunken (red softening) *Later the blood pigments degenerate with the production of* bilirubin and are partly absorbed producing a yellow coloured lesion (yellow softening) Finally much of the softened tissue *becomes necrotic and is absorbed leaving one or several* cystic cavities These cavities are never so sharply defined as those resulting from embolism *because of the more complete necrosis occurring with the later lesion* *Still* a severe arterial thrombosis occurring at an early age may result in a porencephaly Cavities *found in cases of apoplexy after years have elapsed* are too often *attributed to* hæmorrhage in reality they are nearly all due to thrombosis The cerebrospinal fluid in thrombosis is never *found to contain blood but some little time after the* apoplexy it is often coloured yellow or yellowish brown from escape of changed blood pigments when the lesion has reached the *surface of the convexity or the surface* of the ventricle and pleocytosis may be found after a recent softening

Hæmorrhage which is usually described as an apoplexy *of sudden onset may* be so when the escape is from a large vessel When the bleeding commences from a smaller vessel the symptoms *are not sudden in their onset* but gather *rapidly* Such a hæmorrhage is much like an avalanche Commencing from a small vessel the hæmorrhage tears a small cavity *and in so doing opens up fresh bleeding points* and with increasing destruction more and more bleeding occurs from every piece of torn tissue until the hæmorrhage reaches such a size as *to burst commonly into the* ventricle and much more rarely on to the surface Indeed it is difficult to conceive how a hæmorrhage into such a soft and vascular tissue as is the *brain should* ever stop As a matter of fact it rarely does so but causes death in the first attack of hæmorrhagic apoplexy within from a *few hours to a few days after the* onset from widespread

tearing up of the nervous tissue and bursting into the ventricle One of the most important clinical distinctions between apoplexy due to thrombosis and apoplexy due to hæmorrhage is that the former is often survived and that the latter is almost invariably fatal within a short time of the onset

Hæmorrhage may occur anywhere within the nervous system but its common seat of commencement is in the centrum semiovale and the vessel which bursts is one of the perforating arteries of which the lenticulo striate which carries the name of the artery of hæmorrhage is the most common Such bleedings are often called capsular hæmorrhages It must be pointed out that this term capsular refers to the region outside the corpus striatum or external capsule and not to the compact internal capsule as it converges to the crus cerebri The cerebrospinal fluid in cases of hæmorrhage contains blood within a very short time of the onset

While both thrombosis and hæmorrhage may occur in any part of the brain the semi-oval centre the calcarine region and the pons are the common sites of both of them in that order of frequency Hæmorrhage is rare except in these regions while thrombosis is not uncommonly met with elsewhere

Symptoms —The nature of the symptoms in apoplexy will depend upon the site of the vascular lesion and as the semi oval centre is the commonest site and as many arteries supply the fibres of the pyramidal tract in different parts of its course hemiplegia is the common result if the lesion is in the left hemisphere some degree of aphasia is commonly associated with the hemiplegia

Thrombosis of the *anterior cerebral artery* in its distal portion causes paralysis and postural sensory loss in the contralateral leg but if the vessel is thrombosed proximal to the origin of the artery of Heubner—which supplies part of the anterior limb of the internal capsule—the contralateral arm and face are also affected so that hemiplegia results The *middle cerebral artery* is rarely thrombosed as a whole except in syphilitic cases which are now uncommon thrombosis of the whole of this artery causes such extensive destruction in the corresponding cerebral hemisphere that the most severe hemiplegia with postural loss and hemianopia results accompanied by severe aphasia if the lesion is on the left side Both of these arteries may be involved when thrombosis occurs in the *internal or common carotid artery* The frequency of this condition has been disclosed by arteriography In such a large artery the clot is at first mural and portions of it may break off and cause emboli in branches of the derived arteries When the lumen of the internal carotid artery becomes completely obstructed the anterior and middle cerebral arteries continue to receive blood by way of the circle of Willis and even the ophthalmic artery which takes origin just before the bifurcation usually receives a blood supply sufficient to prevent the occurrence of blindness in the corresponding eye While the middle and anterior cerebral arteries may remain patent the blood supply to them through the circle of Willis may be inadequate and especially in elderly subjects successive softenings of greater or less degree may therefore occur in the hemisphere of the affected side It is consequently not uncommon for two or more incidents of partial hemiplegia to occur with intervals of days or weeks or even months between them The severity of the clinical pictures that may result from carotid thrombosis is consequently subject to very great variation but in quite a number of cases the paralysis is surprisingly slight and it is only by arteriography that the condition can be confidently diagnosed In the worst cases, however all the arteries derived from the internal carotid may be thrombosed and the condition may be fatal in the acute stage In some instances both internal carotid arteries have been found to be occluded and these have usually been cases of dementia There is evidence that the thrombosed carotid artery may become recanalised A considerable number of the patients who suffer from carotid thrombosis are men in the first half of life and trauma to the neck may be an important ætiological factor in older patients the condition is usually associated with atheroma

When the *posterior cerebral artery* is thrombosed the outstanding sign is contra lateral *hemianopia with sparing of the fixation point*

Pontine apoplexy involves the appearance of motor and sensory hemiplegia—first on one side and then on the other with the onset of coma, involvement of cranial nerve nuclei *e g* with loss of lateral movements of the eyes—may be the first sign

Cerebellar apoplexies and thrombosis of the *posterior inferior cerebellar artery* produce acute ataxia with forced movements and vomiting (p 1440)

The onset in hæmorrhage is almost always rapid and may be sudden, in thrombosis it may be sudden or ingravescent with embolism it is always instantaneous Consciousness is lost or not, according to the severity of the initial lesion and the site it occupies and to the magnitude of the processes which follow the initial lesion namely the œdema of embolism and thrombosis and tearing of the brain tissue in hæmorrhage In hæmorrhage consciousness is lost soon and the rapid development of severe symptoms which progressively deepen is a most important early indication that this is the nature of the lesion In calcarine thrombosis the initial symptoms may be so slight as to pass unnoticed by the patient whose first indication of defect may be that he runs into objects on his blind side Convulsion sometimes occurs at the onset and this nearly always indicates thrombosis rarely embolism and never hæmorrhage There may be some local spasm in the region of the cranial nerves in pontine hæmorrhage, but this is not convulsion

Conjugate deviation of the eyes is a common feature of all apoplexy When the lesion is irritative at its onset, and not too destructive and always when convulsion occurs at the onset there may be active conjugate deviation the eyes being turned away from the side of the lesion and towards the paralysed or convulsed side in *hemiplegic cases or the blind side when hemianopia is present* But this active conjugate deviation lasts but a short while and is followed by a paralytic conjugate deviation in the opposite direction both eyes being directed away from the paralysed side and towards the side of the lesion This variety of conjugate deviation may last for a considerable time but usually disappears with the onset of deep coma

The pupils are often unequal they may be contracted or dilated widely and may be insensitive to light In severe apoplexy when as the result of the cerebral shock or when hæmorrhage or œdema has so raised the pressure as greatly to reduce the physiological activity of all the intracranial elements with the production of deep coma the pupils are widely dilated and insensitive In pontine lesions the pupils are often contracted to pin point size and this condition is of important localising significance

In proportion to the severity of the general intracranial disturbance respiration tends to be hurried noisy and stertorous and with increasing pressure to become irregular grouped or of the Cheyne Stokes type The blood pressure tends to be raised and the pulse full in all conditions of apoplexy provided the heart will respond to the requirement of an increased blood pressure in the face of an increased intracranial pressure Swallowing is often impossible and the sphincters may be relaxed or retention may occur

In the usual variety of apoplexy where the lesion is in the area of the middle cerebral artery and the local sign of the lesion is hemiplegia it will be obvious that when the general intracranial pressure becomes severe and the coma becomes deep the hemiplegia becomes less apparent or masked by the universal condition of paralysis consequent upon the general intracranial condition The physician often sees the patient for the first time when there is considerable coma and he must determine upon which side the lesion is situated and endeavour to have some perspective as to prognosis by determining the severity of the lesion

The following points will serve to determine the side of the lesion when these signs are present (1) The paralytic conjugate deviation is towards the side of the lesion (2) The corneal reflex when any is present is diminished or lost on the

hemiplegic side (3) Painful stimulation will elicit less response or no response upon the hemiplegic side (hemianæsthesia) (4) The patient may respond by blinking to a feint made with the observer s hands towards the patient s eyes upon the sound side and not on the hemiplegic side (hemianopia) (5) The limbs on the hemiplegic side when raised and allowed to fall passively do so in a more lifeless inert and flaccid fashion than upon the sound side (6) And when there is any difference between the knee jerks abdominal reflexes and plantar reflexes the former tend to be diminished and lost on the hemiplegic side while the plantar reflex will be of the extensor type on the hemiplegic side It must be remembered in this connection that a severe lesion of one cerebral hemisphere abrogates for a time at least most of the functions of the whole hemisphere and that the hemianæsthesia and hemianopia here referred to do not necessarily indicate that the destructive lesion involves the visual and sensory paths And further that the condition of coma due to increased intracranial pressure of itself causes such signs as bilateral loss of abdominal reflexes and knee jerks and bilateral extensor responses in the plantar reflex

The severity of the lesion may be judged—(1) From the depth of the coma (2) from the degree to which the patient responds to any form of stimulation and from the general signs of nervous depression present—for example a condition of complete bilateral flaccidity with complete loss of all reflex action and of all response to stimulation indicates a most severe lesion and (3) from signs of failure of respiration as shown by irregular grouped or Cheyne Stokes breathing It is further important to arrive at a determination if possible as to whether the condition present is stationary deepening or showing signs of amelioration

Vomiting is not an uncommon occurrence in the early hours of apoplexy and before coma becomes deep Hyperpyrexia is often seen in fatal cases before the end It is especially common and may reach a high degree in pontine apoplexy It may be preceded by initial depression of temperature It is of fatal prognostic import

Hemiplegia is the commonest sequel of vascular lesions of the brain The signs which serve to indicate its presence in the comatose subject have already been enumerated After cerebral thrombosis it may happen that the initial hemiplegia is completely recovered from but unless this recovery begins early and progresses rapidly it is not likely to be complete The essential feature of hemiplegia is the loss of voluntary movements on one side of the body, but as this loss begins to pass off certain new features make their appearance These are muscular hypertonus increased tendon jerks and associated movements

The restoration of movements follows a certain order Deviation of the tongue and facial asymmetry clear up early next the leg begins to recover and finally—and often very incompletely—the arm The return of movements in the limbs is selective In both upper and lower limbs movement at the proximal joints recovers first and most completely In the leg extension and plantar flexion recover more completely than flexion and dorsiflexion As a result the patient can often stand when he cannot lift the foot and leg to step properly and has instead to circumduct the limb when walking In the arm flexion movements recover first and best while the fine skilled movements of the hand and fingers are frequently lost for ever

The development of hypertonus or spasticity is as selective as the return of movements In the leg the extensor group of muscles becomes spastic in the arm the flexor group Thus the arm tends to take up a position of adduction with flexion at elbow wrist and digits The leg is always spastic in extension and does not go into flexion contracture as may happen in spastic paraplegia from spinal cord lesions The degree of hypertonus varies and is greatest when the loss of movement is greatest

The tendon jerks are exaggerated and there is clonus (knee and ankle) in the affected limbs The Babinski plantar response persists, but the abdominal reflexes which are initially lost on the affected side sometimes return after a period of months

The forced immobility of shoulder and distal joints in the arm may lead to the formation of adhesions

The so called associated movements are involuntary changes of posture of the paralysed limbs which accompany forceful voluntary movements, or such involuntary movements as yawning

CEREBELLAR APOPLEXY —This is usually the result of thrombosis of the posterior inferior cerebellar artery which is a branch of the vertebral artery and the clinical picture is very unlike that of cerebral apoplexy *The patient is seized with a sudden* intense vertigo which throws him to the ground, as in Ménière s disease Incessant vomiting and forced movements follow the forced movements rotating the patient, so that he comes to rest prone, with that side of the face corresponding with the side of the cerebellar lesion in contact with the pillow There is intense ataxy usually *bilateral at first and later becoming confined to the limbs and trunk on the side of* the lesion The patient is unable to lift his head, or to maintain the sitting or standing position When placed in such a position he positively dives to the ground when released Nystagmus with the long slow movement to the side of the lesion and a short fast movement in the opposite direction is conspicuous and the skew deviation *of the eyes is sometimes seen* There is much general hypotonia of limbs and trunk which soon becomes limited to the side of the lesion Head retraction, pain and stiffness of the neck and opisthotonos may occur When the patient s condition recovers sufficiently to allow of examination all the signs of a unilateral cerebellar lesion will be found Consciousness is not often lost Since the posterior inferior cerebellar artery also supplies the lateral region of the medulla signs indicative of disturbance of this region are usually present and these may dominate the clinical picture rather than the cerebellar signs Chief amongst them are analgesia and ther manæsthesia of the face and head due to implication of the as yet uncrossed quinto thalamic path and of the limbs and body upon the opposite side due to involvement of that part of the spinothalamic tract which has crossed below this level Between these two areas of sensory loss there is often a gap where sensibility is normal corre sponding with that part of the spinothalamic tract which is crossing obliquely at this level and therefore is too near the middle line to be affected Paralysis of the motor vagus is often found from involvement of the nucleus ambiguus and from the exten sion of the lesion or of consecutive œdema towards and across the middle line it sometimes causes severe dysphagia and dysarthria and one of the great dangers of this form of apoplexy is extension of the thrombosis to that part of the medulla which contains the respiratory and other vital centres When however, such extension does not take place, and if the destruction of the lateral lobe is not too extensive the most remarkable recovery may take place

Diagnosis —*The nature of the lesion* —Thrombosis should be diagnosed not withstanding the presence of high arterial tension or renal disease in all cases of apoplexy without organic cardiac valvular disease when the onset occurs during sleep or under circumstances of quiet depletion or exhaustion, and in all cases where prodromal symptoms are marked or where the onset of the apoplexy is gradual and in apoplexies occurring in advanced age for then hæmorrhage is almost unknown All slight apoplexies and nearly all those that survive the first 10 days after the ictus are due to thrombosis Thrombosis should be diagnosed in all primary apoplexies in young syphilitic subjects, and in this connection the serum reaction and the cytology and reactions of the cerebrospinal fluid are all important in the diagnosis

Puerperal apoplexy is mostly due to thrombosis of cerebral veins (see p 1452)

The cerebrospinal fluid affords important indications since hæmorrhage into the brain in most of the cases soon leaks on to the surface or into the ventricle If blood is absent from this fluid a few hours after the ictus thrombosis or embolism is highly probable and *hæmorrhage is very unlikely* Any infarction coming to the surface may in the course of time cause the fluid to be blood tinged or yellow It is

important to bear in mind that the infarct conditions of embolism and thrombosis are followed by packing of the infarcted region with polymorphs and that these may escape from the surface in such numbers as to load the cerebrospinal fluid with such a high polymorph pleocytosis as to suggest the presence of suppurative meningitis

Hæmorrhage is a likely cause of apoplexy occurring during exertion especially if it occurs at a moment of severe physical strain or at the height of passion It is always a probable lesion in cases where a previous thrombotic apoplexy has occurred the final event where multiple strokes have succeeded one another being almost invariably hæmorrhage An apoplexy with rapid onset and with symptoms rapidly deepening with a quick onset of deep coma and the development of pyrexia and signs of respiratory failure is usually due to hæmorrhage The certain test that an apoplexy is due to hæmorrhage is the presence of blood in quantity in the cerebro spinal space as proved by lumbar puncture In cases of chronic nephritis and malig nant hypertension where the blood tension is very high, and where there is severe retinitis hæmorrhage is the most likely cause of stroke

Embolism should be diagnosed in all cases in which there is an obvious cardiac valvular lesion particularly mitral stenosis septic endocarditis aortic disease or aneurysm It is true that syphilitic cerebral thrombosis may occur with syphilitic aortitis but the combination is rare for syphilitic aortitis usually occurs at a much later age than does syphilitic cerebral thrombosis

The position and extent of the lesion —The position of the lesion may be judged by the nature of the initial signs whether visual sensory motor or aphasic cerebellar or pontine and later by the permanent symptoms resulting from the lesion It must be carefully borne in mind in this connection that a severe lesion of a cerebral hemi sphere may entirely abrogate the functions of that hemisphere during the acute stage initially by a process of shock and afterwards by the occurrence of œdema in the vicinity of the lesion which may spread widely The extent of the lesion may be gathered by the severity or otherwise of the early symptoms and their rate of increase, and by early or immediate loss of consciousness and by the completeness of the paralysis resulting The more severe the extent of the lesion the sooner do grave signs of general cerebral failure appear

Differential Diagnosis —The diagnosis of coma due to a cerebral vascular lesion is usually made without difficulty from the history and from the presence of un equivocal signs of local lesion of the brain In a patient without history and when the coma has become so deep as to remove the unilaterality of physical signs the diagnosis may be difficult from other causes of coma such as uræmia and diabetes poisoning by opium alcohol and its derivatives and coal gas and in cases of difficulty search is to be made for the usually obvious signs of these conditions Uræmia may present especial difficulties for it is often associated with cerebral vascular lesion and transient hemiplegic attacks may occur in this condition This is true also of the crises of essential hypertension which are described in more detail on p 1444 Absolutely sudden death which is so often recorded in death certificates as due to apoplexy is usually associated with cardiac infarction Apoplexy never causes sudden death There is one recorded case of death from cerebral hæmorrhage in 5 minutes but it is rare in any apoplexy for death to occur in less than 2 hours Other conditions causing hemiplegia with coma must be taken into consideration Epilepsy especially when the convulsion is unilateral may be followed by marked unilateral paralysis (Todd s paralysis) which may last for a considerable time Here the history of recurring attacks and the complete recovery will easily prevent confusion

Cerebral malaria and heat stroke may closely resemble apoplexy and should always come to mind when rapid coma follows the development of cerebral symptoms in circumstances where these causes are likely The congestive attacks of general paralysis of the insane are peculiarly difficult to diagnose from apoplexy and especially

so when occurring as the initial manifestation of the disease These attacks take the form of rapidly occurring attacks of hemiplegia aphasia hemianopia, hemianæsthesia or of some combination of these conditions usually associated with initial convulsions and followed by coma The diagnosis of a syphilitic thrombosis is made with reason because of the positive serum reactions and cerebrospinal fluid examination If energetically treated the patient recovers with rapidity and completeness It is the too rapid recovery in a case of apparent syphilitic thrombosis which should suggest the possibility of the stroke being a congestive attack in general paralysis of the insane

In all cases of coma without history, especially when there are signs of local cerebral involvement a careful examination of the head should be made for traces of recent injury

Prognosis—In thrombosis due to atheroma the apoplexy may be rapidly fatal from extension of the thrombosis and secondary œdema In cases which survive considerable recovery may occur in proportion to the extent of the lesion but in these subjects an apoplexy is usually the beginning of the end since the underlying pathological causes arterial disease and failing cardiac action still exist and are not amenable to any radical treatment It is astonishing however how many of the cases of apoplexy *due to atheromatous thrombosis survive for years without any recurrence of the thrombosis* or occurrence of hæmorrhage A majority of the cases of apoplexy from syphilitic thrombosis make a fair recovery which obviously depends upon how much permanent thrombosis occurs in the lesion of acute syphilitic encephalitis which is responsible for this condition and upon the early application of appropriate treatment for syphilis In some of these cases even, no recovery occurs

In cases of hæmorrhage the immediate prognosis is the gravest possible the great majority of the cases surviving but a few hours

Treatment—When arterial disease is known to be present, the only measure which can in any way tend to safeguard the patient from apoplexy is moderation in all things in diet alcohol mental and physical exercises and above all moderation in all measures tending to cause marked variation in blood pressure It is highly probable that no treatment influences the course and fatal issue of apoplexy due to hæmorrhage Thrombosis and embolism however allow some scope for treatment which should be the same in the two conditions and as medical treatment in cases of hæmorrhage is useless and cannot avert the fatal result one line of treatment may be recommended in all cases of apoplexy

Absolute rest is in the first place, essential when prodromal symptoms appear Restlessness may be combated with bromides If the patient is conscious he should make as little effort as possible His head and shoulders should be raised special care being taken that the neck is not bent and that nothing shall interfere with the return of blood from the head If there is unconsciousness with stertor the head and shoulders should be turned upon one side so that the tongue does not fall back and impede respiration Purgation should be avoided and the bowel relieved at intervals by enemata Food in a liquid form should be administered at regular intervals and if there is any difficulty in swallowing the food should be administered with the nasal tube The bladder should be carefully watched from the first, lest retention should occur and the catheter passed when necessary Lumbar puncture should when necessary be performed for diagnostic purposes, and it frequently gives relief from symptoms due to the high intracranial pressure Bed sores and hypostatic bronchitis must be avoided by the usual measures In the cases that survive the first few days passive movements should be used daily to all the joints of the affected side in hemiplegic cases for this will obviate the painful residual adhesions which form in the joints of the paralysed limbs, and especially in the shoulder joint and subsequently cause so much pain and misery to the patient With the return of the power of voluntary movement active exercises take the most important place in treatment The final stage of hand and finger movements depends

not alone on the severity of the damage done to the brain but in part upon the thought given to devising active exercises for it and the assiduity with which the patient can be persuaded to employ them To avoid fatigue it is best to ordain a given daily period of some minutes for systematic exercise A rubber sponge of appropriate size fixed in the palm by a strip of webbing passing round the hand will limit the passive flexion of the fingers and will provide a resilient resistance against which the patient may move his paretic digits Massage is an adjuvant but never a substitute for active exercises in the patient who can undertake them Electrical stimulation of the muscles is absolutely contraindicated It has no other effect than to aggravate the spasticity that is so serious a hindrance to free movement A hemiplegic patient after apoplexy, should be got upon his legs and encouraged to make attempts to walk as early as ever the returning power allows any possibility of the attempt

GENERALISED CEREBRAL ATHEROMA

Ætiology and Pathology—For the ætiology and pathology of atheroma the articles on pp 835 919 should be consulted In many subjects the cerebral arteries are affected at an earlier age and more severely than any others in the body Males are the victims of generalised cerebral atheroma more often than females and the symptoms though most common in the sixties and later, are recognisable in the more severe cases soon after the age of 50 The brain is the seat of innumerable minute vascular lesions There are numerous small softenings on its surface and the cerebral cortex becomes thinned in consequence of degenerative changes In the central parts of the brain especially in the basal ganglia small cysts develop from the softenings and eventually a mesh like condition—the status lacunatus—may result

Symptoms—The onset of this condition is insidious and its course steadily progressive Mental or physical changes may predominate and both are liable to abrupt exacerbations which are to be attributed to small cerebral vascular lesions The mental symptoms are often noticeable first The patient s range of interests becomes reduced and intellectual activities of all kinds are gradually discarded Memory for recent events becomes faulty while that for events long past remains unimpaired Confusion is liable to occur and the patients become unable to adapt themselves to new circumstances and are obstinately conservative Emotional control becomes impaired and affective response may be inadequate Previously existing tendencies to anxiety or depression or paranoid traits may become exaggerated Confusion and lack of attention may lead to incontinence and disorders of dress Dysphasia is common and apraxia may also occur

The physical symptoms take the form of a slowly developing muscular rigidity which has been called pseudo Parkinsonism The facies becomes set movements become less free and in walking the step becomes gradually shortened until it may be only a few inches this *marche à petit pas* is very characteristic The patient becomes unable to relax his muscles and if as he lies in bed passive movements of the limbs are attempted by the examiner great resistance is encountered The grasp reflex may be discovered in one or both hands The tendon jerks are exaggerated and the plantar reflexes indefinite or weakly extensor

In some instances the most pronounced physical feature is a spastic paralysis of the muscles innervated from the pons and medulla and hence called pseudo bulbar-palsy The physical basis of this syndrome is uncertain the lesions concerned are bilateral and may be situated in the anterior parts of the internal capsules or possibly in the brain stem itself The facies becomes set voluntary movements of the lips are restricted the tongue is spastic and looks small and cannot be protruded beyond the teeth and movements of the palate pharynx and vocal cords are all

similarly limited The result is dysarthria of a degree which *may render the patient's speech unintelligible* together with difficulty in mastication and in swallowing (dysphagia) There is no muscular wasting The jaw jerk *is exaggerated The* lips may be held apart and the saliva trickles from between them Emotional movement temporarily inhibits the rigidity of the facies and is exaggerated as a consequence of the pyramidal impairment Moreover, in consequence of the bilateral pyramidal disturbance uncontrolled laughter or crying may occur and there is usually a tendency towards one or the other so that the patient who suffers *from uncontrolled* laughter may laugh even on hearing bad news and the patient who suffers from uncontrolled crying may weep when he is amused General atheroma is usually well marked and arterial hypertension may or may not be present The state of the retinal arteries is not a reliable guide to that of the cerebral arteries

Diagnosis —If mental symptoms predominate in the early stages the diagnosis will have to be made from general paralysis of the insane and the absence of characteristic signs of nervous syphilis, together with negative findings in the blood and cerebrospinal fluid will exclude the latter Other forms of pre senile dementia such as Alzheimer s disease (see p 1630) and Pick s disease (p 1629) are not associated with the same degree of motor disturbance as is usual in atherosclerotic dementia When physical symptoms predominate the presence of atheroma and signs of early dementia and usually the absence of tremor differentiate the condition from paralysis agitans When pseudo bulbar palsy is present, the diagnosis from motor neurone disease (amyotrophic lateral sclerosis) may be difficult but the complete absence of wasting the presence of rigidity in the facies and upper limbs and the association of atheroma are usually sufficient to make the distinction When arterial tension is high and changes in the optic fundi are present the picture may closely resemble one of cerebral tumour, and the differentiation depends largely on the presence of arterial hypertension and the extensive retinal lesions which distinguish neuro retinitis (hypertensive neuro retinopathy) from the papillœdema of raised intracranial pressure

Prognosis —The course of the disease is gradually downward and may at any time be terminated by a severe stroke ' but in general the patients survive for years and severe cerebral vascular accidents are uncommon among them In the end the patient becomes bed ridden and dies in consequence of an intercurrent infection or when he has reached a debilitated state from a terminal cerebral thrombosis

Treatment —This can only be symptomatic and the patient should be kept up and about as long as possible It is unfair and unwise to put too much dietary restriction on him and if he is a small or moderate eater no further limitation is required

HYPERTENSIVE ENCEPHALOPATHY

In a preceding paragraph on the differential diagnosis of apoplexy (p 1441) mention was made of the sudden and transient cerebral symptoms associated with essential hypertension and some further reference to them is necessary It is known that the subjects of this variety of hypertension may ultimately succumb to cerebral hæmorrhage but it should also be borne in mind that they are subject from time to time to what are known as hypertensive crises Similar attacks occur in acute nephritis and eclampsia The patient has a high blood pressure The attack is precipitated by a further rise in this and develops with intense headache sickness and sometimes drowsiness or even semi coma Examination will reveal the presence of hypertensive retinitis in most cases but in a proportion there is a definite papill œdema with retinal hæmorrhages and exudate Accompanying these symptoms there may be hemiparesis hemianopia focal or generalised fits or other indications of a local cerebral lesion The crisis is brief lasting from a few hours to several days and usually ends in recovery but recurrence is likely and finally many subjects develop

cerebral atheroma and succumb to cerebral hæmorrhage Intervals of several months may intervene between succeeding crises

The presence of papillœdema is taken to indicate that cerebral œdema is complicating the situation The transient nature of the crisis and particularly the rapid appearance and disappearance of such symptoms as hemiparesis exclude the possibility of arterial thrombosis or other material lesion of the kind and spasm of the arteries has been invoked to account for the symptoms There is no conclusive evidence that this occurs Yet while the cerebral arteries are not under the same measure of vasomotor control as arteries elsewhere in the body, it is known that some such control exists and it may be that in arterial hypertension more intense spasm is possible than in healthy arteries At least it may be said that no hypothesis better founded or more in harmony with the facts of clinical observation has been formulated

Differential Diagnosis —As has been indicated the transitory character of the symptoms excludes gross vascular lesions such as thrombosis and the same may be said of intracranial tumour and lead encephalopathy Yet it may be admitted that while it is present the hypertensive crisis shows many points of resemblance to the last two named conditions especially when papillœdema is found Plumbism in children and young persons not uncommonly develops with headache vomiting convulsions and focal signs and the development of an intense papillœdema sometimes also with high blood pressure and albuminuria and search for other indications of lead poisoning and careful history taking are necessary to exclude this condition In intracranial tumour the systolic blood pressure is rarely above normal limits the history is longer and the condition progressive Uræmia can usually be excluded since in essential hypertension the blood urea is within normal limits and the only abnormality in the urine may be a trace of albumin

Treatment —Venesection is indicated as the first step and when there is papillœdema or other signs of cerebral œdema (convulsions high cerebro spinal fluid pressure) lumbar puncture and the withdrawal of cerebrospinal fluid and also the intravenous or intramuscular administration of hypertonic solutions are necessary As a measure of urgency from 50 to 70 ml of a 50 per cent solution of dextrose or sucrose may be given intravenously For less urgent cases and as a measure that can be repeated for the relief of headache 6 oz of a 20 per cent solution of magnesium sulphate may be given per rectum at 6 hourly or less frequent intervals The convulsions may be treated by rectal administration of paraldehyde (240 to 360 minims in water) or by the hypodermic injection of gr 3 of soluble phenobarbitone in solution

The subsequent management of the case is that of the underlying essential hypertension it should be borne in mind that the use of potent detensive drugs in patients with diseased cerebral vessels is accompanied by a great risk of thrombosis

CEREBRAL EMBOLISM

Cerebral embolism is infinitely less common than thrombosis

Ætiology —The embolus may be (1) a fragment of blood clot (2) a vegetation or detached portion of one of the cardiac valves or in rare instances an atheromatous plaque (3) air bubbles or (4) globules of fat

(1) The commonest cerebral embolus is a detached fragment from a clot which has formed in the left auricle in a case of auricular fibrillation Less frequently it comes from a clot in the dilated auricular appendage in a case of mitral stenosis without fibrillation or from one on the inner surface of the infarcted ventricular wall after coronary thrombosis Other sources of clot emboli are aneurysms of the large vessels between the heart and the brain a clot covering an atheromatous ulcer in the first part of the aorta and clots which may form in the pulmonary veins and even in

the left heart in suppurative conditions of the lungs In exceptional cases a congenital heart lesion may provide a route by which emboli from the systemic veins can reach the brain without passing through the lungs—paradoxical embolism (see p 697)

(2) The emboli of the second group are most commonly small portions of infected vegetations from the cardiac valves in cases of subacute bacterial endocarditis In other instances larger emboli are formed by vegetations from acute bacterial endocarditis

(3) Air emboli are usually multiple They may occur in association with operations on the lungs and in the course of almost any operation in which a vein of medium or large size is opened While emboli of more solid character will not pass through the pulmonary capillaries it is probable that air emboli do so and consequently air emboli from almost any part of the body may reach the cerebrum. The commonest single cause of air embolism to day is probably damage to the surface of the lung by the needle in the course of producing or refilling an artificial pneumothorax and it occurs also during major operations on the lung It may follow insufflation of air into the vagina or it may occur in association with retained placenta and even as a result of division of veins during the operation of Cæsarean section

(4) Fat emboli are a cause of cerebral complications after fracture of one of the long bones and may cause death Like air emboli fat globules pass through the pulmonary filter

Emboli usually pass into the middle cerebral arteries or their branches because these are the direct continuation of the carotid arteries Very rarely the internal carotid is obstructed but if it is the circulation in its branches is usually maintained by the circle of Willis Next in frequency is the posterior cerebral artery, and then the vertebral Because of the mode of origin of the left carotid artery, emboli affect the left half of the brain more frequently than the right In a case of subacute bacterial endocarditis the cumulative effect of innumerable minute infected emboli may cause extensive softening in the left hemisphere at a time when the right hemisphere is little affected

Symptoms—The onset is immediate A stroke due to embolism is the most suddenly occurring of all the apoplexies and there are no prodromal cerebral symptoms Unless a large vessel such as the middle cerebral artery be occluded consciousness is usually not lost but a stuporose state may occur either with the onset or after a few hours, and may last several days Hemiplegia is the common physical syndrome and it may be of all degrees of severity according to the size of the cerebral lesion When emboli are numerous and of small size and particularly when they are infected as in subacute bacterial endocarditis the development of hemiplegia may be gradual

Diagnosis—Embolism should never be diagnosed unless there is evidence of cardiac disease aneurysm or some other recognised source of emboli but in the presence of such disease especially of auricular fibrillation it is the usual cause of any stroke which may occur The diagnosis should not be rejected simply becau e the manifestations of apoplexy are slight

Prognosis—In cases of auricular fibrillation the hemiplegia is in many cases not severe and good recovery is frequent but when a large vessel is occluded the hemiplegia is usually very severe and complete and it remains so Further embolism is likely to occur eventually In other cases the prognosis depends largely on the course of the causal condition which is responsible and whether the emboli are affected or not In cases of bronchiectasis for example, the emboli being infected generally give rise to multiple cerebral abscesses Puerperal cases of cerebral embolism in the absence of cardiac and other disease usually do well

Treatment—As far as the cerebral lesion is concerned treatment is the same as for thrombosis In most cases the condition responsible for the embolism calls more urgently for treatment and in cases of auricular fibrillation complete rest for

several weeks and appropriate treatment of the cardiac disorder is essential, in order to diminish the risk of further emboli occurring

INTRACRANIAL ANEURYSM

Aneurysms within the cranium are common and may conveniently be considered in four groups

(1) Minute atheromatous aneurysms of the arteries at the base of the brain are frequent and may be numerous in elderly subjects but only in rare instances do they cause symptoms The clinical disturbances to which they occasionally give rise result either from bleeding or from their pressure on and even adhesion to the adjacent ocular nerves, and are thus similar to those of the more important group which follows

(2) Of the remainder the great majority are berry aneurysms situated on or near the circle of Willis An aneurysm of this kind develops at a bifurcation of an artery in consequence of a congenital defect in certain individuals of the elastic lamina at this point It is thus not congenital but develops at the site of a congenital weakness The importance of berry aneurysms is that they may and frequently do rupture causing subarachnoid hæmorrhage Otherwise only a small proportion of them give any evidence of their presence Aneurysms situated on the posterior or lateral portions of the circle may interfere with the third cranial nerve giving rise to paralysis which is as a rule partial and which may be either gradual or sudden in its onset Less commonly aneurysms situated laterally on the circle compress the optic tract just behind the chiasma and so produce homonymous defects in the visual fields and in rare instances aneurysms on the anterior communicating artery cause pressure on the optic chiasma with consequent disturbance possibly of variable intensity in the central or temporal parts of the visual fields

(3) Aneurysms of the internal carotid artery are usually situated within the cavernous sinus Such an aneurysm may develop gradually or more commonly after an initial period of slow development it may dilate rapidly or even suddenly until it comes into contact with the wall of the sinus or again it may rupture into the sinus becoming an arterio venous aneurysm (see also p 929) Whether the development of the aneurysm be slow or rapid the various oculo motor nerves and the branches of the trigeminal nerve situated in the wall of the sinus become affected The patient experiences severe pain in one side of the forehead or in the forehead and cheek and if the onset is sudden he may vomit Double vision comes on rapidly and may proceed to complete paralysis of the third fourth and sixth cranial nerves but the paralysis is more often partial Ptosis is always a feature The affected eye may become proptosed When the lid is raised the patient may find that vision in the affected eye is impaired but in some cases within a few days the vision improves greatly and the pain passes off some ocular paralysis and proptosis usually remaining If the aneurysm is situated above the cavernous sinus (supra clinoid carotid aneurysm) the optic nerve may be affected by direct pressure and progressive visual impairment may be the first symptom By suitable radiographic technique erosion of the great wing of the sphenoid or of some part of the sella turcica may be demonstrated or some degree of calcification may be seen in the wall of the aneurysm Aneurysms of the internal carotid artery may be demonstrated also by arteriography In cases in which there is an arterio venous communication a bruit may be audible with the stethoscope either over the affected eye or over the carotid artery in the neck Such cases are frequently treated by ligation of the common carotid or of the internal carotid artery after a trial period of compression

(4) *Angiomatous Malformations* —The frequency of angiomas of the racemose or cirsoid type has been revealed by arteriography They occur most often in

the territory of the middle cerebral artery and are almost invariably arterio venous racemose aneurysms—that is to say instead of a capillary bed, a tangle of blood vessels is interposed between the arterial and venous systems the arteries feeding the malformation are hypertrophied and dilated and the veins draining it are dilated and pulsating and they contain arterial blood As most of the arteries enter the cerebral hemispheres from the surface these angiomata typically appear on the surface and extend in a sector, often with a roughly pyramidal shape deeply into the hemisphere and may reach to the ventricle Cerebral tissue is found between the vessels of the mass and cerebral tract evidently pass through it without being affected until hæmorrhage or thrombosis occurs There is some evidence that these angiomas gradually enlarge The vessels composing the angioma are not perfectly formed arteries but are vascular channels of very imperfectly differentiated structure for the most part they have very thin walls of irregular thickness composed chiefly of fibrous tissue with some fragmentary and irregularly distributed muscular coat and even wisps of elastic tissue in their walls

These angiomas threaten the lives of their hosts by hæmorrhage and the hæmorrhage may be either intra cerebral or extra cerebral (subarachnoid) or both It may occur at any age from childhood onwards and it is rare for an affected patient to reach middle age without having suffered a hæmorrhage In many cases fits of some kind local or general precede signs of hæmorrhage and sometimes occasional fits occur over many years A symptom which is typical but by no means constant is a systolic bruit it may be heard with the stethoscope all over the head or only over the carotid arteries and in most cases it is at times audible to the patient Headaches are common and occasionally are of a typically migrainous type and associated with vomiting, in other cases they are associated with a feeling of stiffness in the neck and are suggestive of slight leakage from the aneurysm Until hæmorrhage or thrombosis occurs there are usually no abnormal physical signs to be found on clinical examination When the combination of symptoms is suggestive arteriography is called for and the diagnosis is dependent on this procedure

In a special group of cases there is an external as well as an internal angioma the external manifestation being usually situated in the territory of the trigeminal nerve (Sturges Weber syndrome)

A considerable proportion of these malformations (other than the Sturges Weber group) are amenable to surgical removal or palliative ligation of vessels

In rare instances similar malformations occur in the brain stem and by reason of the aggravations which result from small hæmorrhages and the consequent remissions the clinical course of the patient s illness may be very similar to that of disseminated sclerosis

SUBARACHNOID HÆMORRHAGE

Synonyms —Spontaneous Subarachnoid Hæmorrhage, Meningeal Hæmorrhage

Bleeding into the subarachnoid space may be an accompaniment of head injuries and it may also follow intraventricular hæmorrhage but the usual cause of uncomplicated, or as it is sometimes called spontaneous subarachnoid hæmorrhage is rupture of a cerebral aneurysm on the circle of Willis or on one of its component arteries What has been called here the berry aneurysm may rupture suddenly and freely with the production of fatal apoplexy or there may be recurrent leaking of blood in small amounts from such an aneurysm, leading to a syndrome of meningeal irritation Whereas with cerebral hæmorrhage the bleeding occurs into the substance of the brain and the latter is severely and irrevocably damaged with subarachnoid hæmorrhage the blood is effused chiefly outside and over the surface of the brain and although there is still a risk that the immediate consequences of the apoplexy may be equally disastrous if the event is survived the chances of full recovery are infinitely greater

(1) *The apoplectic syndrome*—The patient may have been subject to frequent headaches or the episode may be quite unheralded until a sudden intense headache rapidly followed by sudden lapse into unconsciousness signals the free rupture of the aneurysm It may be thought that an ordinary cerebral hæmorrhage has occurred when the comatose patient is first seen but in uncomplicated subarachnoid hæmorrhage examination reveals no evidence of hemiplegia On the other hand a bilateral Babinski plantar response will be obtained and there will be marked neck rigidity At first both pupils may be small and sluggish but in fatal cases the pupils ultimately dilate Examination of the optic *fundi* may reveal sub hyaloid hæmorrhage or papillœdema Lumbar puncture produces a fluid that resembles pure blood

Recovery from hæmorrhage of this severity is by no means uncommon In fatal cases death commonly ensues within 24 to 36 hours or at some time during the first fortnight from fresh bleeding If this period be safely passed the prognosis as to recovery becomes good The course of the illness may however be prolonged The patient gradually recovers from coma taking possibly many days to regain full and continuous consciousness The temperature rises after 24 hours and remains at 99 5 or 100 F for about a week and the urine may contain abundant albumin and some sugar—either of which may lead to an erroneous diagnosis if the possibility of its occurrence be not known

Headache is intense and may last for 2 or 3 weeks with irritability and some stiffness of the neck The knee jerks or ankle jerks or both are commonly abolished a few days after the onset but they return after a further week or two and in slighter cases sooner The patient who has recovered from his coma shows at first little intellectual activity but answers rationally and briefly when questioned A few weeks later however he is liable to manifest psychotic disturbances of the Korsakoff type having no recollection of his visitors when they come again and giving them confabulatory accounts of his imaginary doings which show that he is disorientated in place and time This disturbance soon passes off completely and in some cases is almost ephemeral and the patient eventually regains his full intellectual powers

From such a severe illness not every patient rises unscathed Focal damage may be caused either by the hæmorrhage or by subsequent clotting If the aneurysm lies close to or partly embedded in the brain its rupture may cause considerable cerebral laceration which if not fatal may leave partial hemiplegic weakness If the aneurysm be at the bifurcation of the basilar artery clotting in or around it may give rise to thrombosis in one of the branches entering the brain stem with resultant motor or sensory hemiplegia of the opposite side of the body associated possibly with oculo motor paralysis on the side of the new lesion Oculo motor palsies also arise from involvement of the nerves in clot and strabismus is perhaps the commonest residual defect

(2) *The meningitic syndrome*—In this case the hæmorrhage is less abundant and therefore consciousness may not be lost There is violent headache restlessness delirium rigidity of neck and spine Kernig s sign bilateral extensor plantar re sponses and sometimes diplopia and squint Within a few hours or somewhat later ophthalmoscopic examination may reveal the presence of flame shaped hæmorrhages in the nerve fibre layer of the retina or massive hæmorrhage in the sub hyaloid space The last named is characteristic of subarachnoid hæmorrhage A low grade papill œdema is occasionally also observed

In small leaking hæmorrhages the cerebrospinal fluid is more or less heavily bloodstained and may for 2 or more weeks be discoloured yellow or brownish according to the amount of blood originally present

(3) *The lumbago sciatica syndrome*—This uncommon condition first described by Hall commences with pain and stiffness in the lumbar region followed by pains in the legs and sometimes the leg jerks are absent Pyrexia is the rule The diagnosis

depends upon the characteristic cerebrospinal fluid of subarachnoid hæmorrhage The explanation of this syndrome is not clear and it is probable that in some cases at least the source of the hæmorrhage is in the spinal canal

Differential Diagnosis —The recognition of subarachnoid hæmorrhage is an easy matter in those cases in which the train of symptoms calls at once for the examination of the cerebrospinal fluid and blood is found in the fluid Prior to lumbar puncture the distinction from other varieties of cerebral hæmorrhage can often be made (1) by the age of the patient practically all hæmorrhagic apoplexy in the first half of life being the result of ruptured aneurysm and (2) by the history of preceding symptoms such as headache diplopia ophthalmoplegia and migrainous phenomena Arteriography performed as soon as the patient is well enough may demonstrate the aneurysm

Prognosis —When the aneurysm ruptures frankly and widely and the bleeding can be free the outlook is hopeless, and death occurs in from a few minutes to a few hours nor does drainage avert the consequences of so large an opening into a main arterial trunk If as so commonly happens there is a slower leakage which perhaps is intermittent the outlook will depend (1) upon the cessation of the bleeding and the healing of the leak by clotting and (2) upon the possibility of the free escape of the effused blood into the subarachnoid space In many of the cases of subarachnoid hæmorrhage the bleeding ceases and healing of the aneurysm by clotting and calcification, occurs with complete recovery In other cases there may be repeated attacks of leaking at intervals of weeks months or even years and again, many of such patients make good recovery in the end

Treatment —In the case of subarachnoid hæmorrhage the patient must be kept absolutely at rest with the administration of sedatives An immediate injection of morphine is indicated when the patient is not comatose and has the usual intense headache It may be necessary also on the recovery of consciousness on account of headache and restlessness In general repeated lumbar puncture is inadvisable as it may lead to recurrence of hæmorrhage but if there be signs of raised or of rising intracranial tension (and progressive slowing of the pulse is generally a reliable indication of this) then lumbar puncture may be expedient When recovery sets in the patient should still be kept in bed for at least 4 and possibly 6 weeks During the first fortnight recurrent hæmorrhage is more likely to occur than later during the course of convalescence When the aneurysm is appropriately situated ligation of the common carotid artery of the same side is sometimes performed and in a few instances the neck of the aneurysm itself has been ligated or clipped

CHRONIC SUBDURAL HÆMATOMA

Synonym —Pachymeningitis Hæmorrhagica

Ætiology —This condition is a consequence of hæmorrhage from veins The latter name now superseded expressed the belief that it was inflammatory and it was supposed that it was more or less confined to chronic alcoholic subjects and sufferers from general paralysis of the insane

It is now known that the lesion is traumatic in origin and is the result of venous hæmorrhage Falls especially those on the forehead or occiput not at the time apparently productive of serious injury may yet cause tearing of the cortical veins as they pass from the surface of the brain to enter the dural sinuses The tear is commonly in the subdural space on one or both sides of the vertex Thereafter blood leaks from time to time from the torn veins and collects on one or both sides of the vertex external to the arachnoid membrane Though by no means unknown in young subjects this type of lesion is much commoner in patients over 50 years of age

Pathology—The periphery of the clot formed tends to organise so that a fine capsule is built up round the hæmatoma The latter remains liquid in its centre, and such hæmatomas may reach a large size The underlying cerebral hemisphere collapses in a peculiar way downwards and medially and the brain stem is thereby pushed over to the other side so that the margin of the crus which contains the pyramidal tract may be indented by the free edge of the tentorium against which it is pressed As a result of this interference with the pyramidal tract of the opposite side a hemiparesis may be caused on the side of the hæmatoma

Symptoms and Diagnosis—The difficulty which still frequently surrounds the diagnosis of subdural hæmatoma depends in large measure upon a general unawareness that it is a not uncommon lesion and from a survival of the old and now obsolete notion that its occurrence is largely confined to sufferers from the two affections named above It must be emphasised again therefore that subdural hæmatoma may follow an apparently trivial head injury in persons at all age periods that essentially its symptomatology is that of a space occupying lesion with a feature characteristic of hæmatoma namely a remarkable fluctuation in the course and severity of the symptoms that owing to the frequently bilateral nature of the lesion the signs are apt to be difficult of localising interpretation and finally that in the presence of such a blurred picture a history of head injury some days weeks or even months before the onset of symptoms should always give rise to the suspicion that a hæmatoma and not a new growth may be present

There is almost invariably a latent period in the development of a subdural hæmatoma This may vary from a matter of days to one of weeks or months On the whole it may be said that in young persons the latent period is apt to be shorter and the symptoms more severe and of more rapid evolution than is commonly the case in elderly subjects In young subjects too there is usually no difficulty in obtaining a history of head injury either a fall upon the head or a blow sustained at sport or in some other way The initial symptom is usually headache fluctuating in intensity apt to be most severe on awaking in the morning or on physical exertion With the passage of days or weeks this becomes more severe and soon other symptoms are added to it The patient has days on which he is drowsy He may pass rapidly into stupor or even coma emerging again to become almost normal Transient accesses of diplopia with squint may be noted Examination during a period of maximal symptoms may reveal a papillœdema sometimes severe in rapidly developing cases The plantar responses may on one or both sides be of the extensor type There may be an inequality of tendon jerks on the two sides the abdominal reflexes may be diminished on one or both sides They may even be absent Periods of mental confusion may also occur In most instances there is no trace of blood in the cerebrospinal fluid

The fluctuation in the severity of the symptoms the fugitive character of the physical signs and the generally downhill tendency of the illness despite the fluctuations are amongst the features which are characteristic of subdural hæmatoma and help to differentiate it from that of intracranial new growth When the syndrome develops rapidly it is more common to meet a marked slowing of the pulse than in new growth

Simple radiographic examination of the skull usually shows nothing more than marked displacement of the pineal shadow to one side or laterally and downwards but if the patient s condition be not so critical as to forbid it examination after injection of air into the theca (by the lumbar or cisternal route) reveals the outline of the hæmatoma and of the deformed cerebral hemisphere while cerebral arteriography gives a striking and characteristic picture that is diagnostic

In all cases there is a great liability to a rapid development of coma with a fatal issue Yet the occasional finding at necropsy of what is clearly a subdural hæmatoma of very long standing unsuspected during life shows that from time to time the

sequence of events briefly reviewed above fails to develop It must, however be confessed that even in such cases it is highly probable that careful clinical examination and an awareness on the part of the examiner of the symptom complex of hæmatoma might have made diagnosis possible during life

Treatment—The features which should make clinical diagnosis possible have been described but in the absence of arteriography certainty can be obtained only by an exploratory operation This consists in bilateral trephine holes and tapping of the subdural space, and if necessary in the turning down of osteoplastic flaps and the evacuation of the cyst when found It is clear that treatment is essentially surgical

THROMBOSIS OF CEREBRAL SINUSES AND VEINS

Thrombosis of the cerebral sinuses or veins may occur as a primary condition or it may be secondary to infective processes spreading to the sinuses from contiguous infected regions

Ætiology—Primary thrombosis is a rare condition It is said to affect the superior longitudinal sinus most commonly It is more common in the first year of life than at any other period when it may follow diarrhœa bronchitis or the conditions of exhaustion met with in tuberculous disease and in congenital syphilis, and it may follow acute diseases, such as measles diphtheria etc It may also occur at any age up to advanced old age, in the terminal stages of cancer pulmonary tuberculosis and other chronic diseases It occurs in the puerperium the antecedent confinement usually having been quite normal and similarly it may occur after abortion

The essential cause of secondary thrombosis is the advent of micro organisms to the sinuses The infection is often a mixed one but the common organisms present are streptococcus pneumococcus and *Bacillus coli* The sinus may become infected as a part of a general pyæmia or infection may spread directly through its wall from a focus of local disease most commonly from an extradural abscess due to ear disease or frontal sinusitis In most cases however the sinus becomes infected from a local spreading septic thrombosis of the veins which open into the sinus from an infected spot at a distance Thrombosis of sinuses may also occur from injury as by bullet wounds and fractures of the skull and may also result from surgical procedures in the region of the sinuses

In the condition known as *otitic hydrocephalus* (see p 1404) a sterile mural clot or deposit of fibrin beginning in the lateral sinus above an infected middle ear extends into the superior longitudinal sinus or spreading sterile clot may obstruct both lateral sinuses and consequent interference with the absorption of cerebrospinal fluid gives rise to hydrocephalus

Pathology—The affected sinus if filled with clot is distended and bulging and feels to the touch as if it were injected with a solid mass In many of the non infected cases, however the clot does not fill the sinus This applies particularly to the superior longitudinal sinus, where there may be extensive mural clot with retention of a blood channel One or several veins draining into the sinus may become obstructed and thrombosed and in cases in which the sinus is filled with clot all the veins entering it may suffer blockage and thrombosis Thrombosis of a vein causes intense congestion of the convolutions which it drains and a moderate degree of subarachnoid hæmorrhage due to rupture of the small tributary veins The underlying brain softens on its surface and later a saucer shaped depression is left at the site The cavernous and lateral sinuses do not drain the brain directly and blocking of one of them does not cause so much cerebral disturbance as obstruction of the superior longitudinal sinus Thrombosis of the cavernous sinus may however extend to the ophthalmic veins and cause blindness and at the same time the nerves which lie in its outer

wall—the third the fourth, the ophthalmic division of the fifth and the sixth nerves—may be paralysed

In the infective forms the clot very quickly breaks down into pus, and general pyæmia results or the spread of infection along a tributary vein may give rise to a cerebral abscess

Symptoms—Many cases are infective and the clinical picture is greatly complicated by (1) the presence of infective disease in relation to the cranium e g in the ear and especially by (2) the onset of pyæmia The symptoms due to thrombosis of individual sinuses or of cerebral veins are more easily recognised in the non infective or primary cases

Superior longitudinal sinus—This sinus has two functions (1) it is a channel into which drain the veins from the upper and medial surfaces of the cerebral hemispheres and (2) by the Pacchionian bodies associated with it it forms part of the mechanism by which the cerebrospinal fluid is absorbed into the blood stream Complete obstruction of the sinus by a clot gives rise to (*a*) extensive bilateral venous thrombosis on the surface of the brain with resulting spastic paralysis of the legs and upper arms the hands and face being spared and (*b*) increased intracranial pressure and in most cases some degree of papillœdema In many cases however the clot does not obstruct the sinus Mural clot may obstruct one or more of the entering veins and thus give rise to hemiplegia which may or may not be ushered in by convulsions or again bilateral paralytic phenomena of any degree may occur There may be associated drowsiness or coma On the other hand the veins may not be obstructed and the clot may be so situated as to interfere with the absorption of cerebrospinal fluid through the Pacchionian bodies paralytic phenomena are then absent and the disturbance is limited to the manifestations of raised intracranial pressure—headaches papillœdema and in some cases vomiting In otitic hydro cephalus the symptoms of this group alone are present

Lateral sinus—It is doubtful whether aseptic thrombosis of one lateral sinus gives rise to any symptoms *provided the other one is of normal size and communication* at the torcular is free Since the superior longitudinal sinus usually turns into the right transverse sinus obstruction of the right lateral sinus may produce a moderate degree of hydrocephalus with headaches and papillœdema In most cases of lateral sinus thrombosis however the clot is infected and manifestations of pyæmia rapidly ensue Meanwhile the clot may extend into the jugular vein and cause pain and stiffness in the side of the neck and occasionally the thrombosed jugular vein may be felt beneath the anterior border of the sterno mastoid as a tender solid cord There may be tenderness and swelling over the region of the mastoid emissary vein and the cervical lymph glands may be enlarged If when Queckenstedt s test is performed the jugular veins are compressed separately compression of the vein on the side of the obstructed sinus causes little or no rise in the manometer whereas compression of the other gives a normal result

Cavernous sinus—Thrombosis of this sinus is usually consequent upon septic spots or injuries on the face sepsis in the frontal sinus or orbital cellulitis Ordinarily the thrombus is infected There is œdema of the orbit with proptosis and œdema of the conjunctiva forehead and face Amblyopia or blindness is the rule but the appearance of the fundus of the eye usually remains normal until the late stages Paralysis of the ocular muscles and anæsthesia of the eye may also occur The condition usually becomes bilateral within a day or two

Diagnosis—This usually depends on the presence of some of the conditions with which sinus or venous thrombosis is known to be associated The possibility of clot in the superior longitudinal sinus and related veins should always be considered (1) *when any convulsive or paralytic phenomena comes on within a month* of childbirth or abortion (2) when in an elderly or debilitated patient manifestations which may include alexia and visual disorientation suggesting vascular lesions on

the two sides of the brain occur within a few days of each other (3) when signs of hydrocephalus appear in association with or soon after an attack of otitis media, and there are no other indications of cerebral abscess and (4) when paralytic or convulsive phenomena occur soon after an injury near the vertex of the skull

Lateral sinus thrombosis is almost exclusively associated with ear disease and its presence can usually be confirmed by Queckenstedt s test Thrombosis of the cavernous sinus presents such a characteristic picture that if an exciting cause is present the diagnosis is seldom in doubt

Prognosis —In the non infective cases the prognosis as regards life is usually good The paralytic phenomena generally make great and often complete recovery within a few weeks but in the severe cases spasticity in the legs and upper arms may be left Blindness or impairment of vision may follow cavernous sinus thrombosis As to the infected cases the prognosis formerly ominous has been greatly improved by the introduction of the sulphonamide drugs and penicillin With lateral sinus thrombosis recovery usually follows prompt operation

Treatment —In the non infective cases the first indication is to allay convulsions if present and doses of soluble phenobarbitone up to gr 3 at a time may be administered by intramuscular injection or by mouth if that is possible Anticoagulants may be employed to prevent the spread of thrombosis but they should be used with full knowledge of the risk of toxic effects (see p 847) For the paralytic phenomena the treatment is identical with that of cases of cerebral arterial thrombosis

The infective cases should be treated immediately as cases of septicæmia and if the local exciting conditions are likely to involve any collection of pus such as an epidural abscess appropriate prompt surgical measures should be taken

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

Before the War of 1914–1918 syphilis was responsible for far more cases of organic nervous disease than any other single factor but during the last 40 years the incidence of neurosyphilis in the United Kingdom has shown a steady decline until it is now less than a tenth of what it formerly was

It is known that in many cases of syphilis the meninges become infected with the syphilitic organism early in the secondary stage but in most cases especially if adequately treated this infection dies out within a year or two In a number of patients however it persists and may become very resistant to treatment After an interval which is seldom less than 2 years syphilitic disease of the meninges and of the blood vessels of the central nervous system may give rise to symptoms and in other instances after an interval varying between 5 and 30 years disease of the cerebral parenchyma may become manifest as general paralysis of the insane or degeneration of fibres in the posterior nerve roots and spinal cord may give rise to tabes dorsalis

In meningeal and vascular syphilis the lesions are composed of miliary gummata They commence with the collection of spirochætes in the spaces surrounding the small arteries and this is followed by an inflammatory reaction with œdema and the exudation of many lymphocytes and plasma cells around the small vessels These cells may wander freely into the nervous tissues away from the vessels and may form clumps often containing giant cells and these too are miliary gummata The initial periarteriolar inflammation is followed in many instances by invasion of the whole vessel wall (panarteritis) and often the most conspicuous feature in such panarteritis is a proliferative endarteritis which may give rise to thrombosis

The sequence of events in the primary degenerative processes in parenchymatous

syphilis is less well known and these processes are as yet unexplained In only one form of nervous syphilis namely general paralysis of the insane is *Treponema pallidum* found in the parenchymatous elements of the central nervous system

In cases of neurosyphilis the Wassermann reaction is usually positive in the blood The most frequent exceptions to this are in cases of tabes dorsalis in which disease the blood Wassermann reaction is negative in about 30 per cent of cases

The cerebrospinal fluid in neurosyphilis shows typically a group of changes, comprising lymphocytosis excess of albumin and a positive Wassermann reaction The Wassermann reaction may however be negative in the fluid when it is strongly positive in the blood and this combination is commonly met with in cerebral meningo-vascular syphilis It is thus essential in all cases in which syphilis is a possible cause of central nervous symptoms to examine the Wassermann reaction both in the cerebro spinal fluid and in the blood, since either may give a positive result when the other is negative In some cases of neurosyphilis particularly tabes the cerebrospinal fluid is normal in every way

GENERAL PARALYSIS OF THE INSANE

Synonym —Dementia Paralytica General Paresis

Definition —This is a progressive disease of the brain due to syphilis causing mental and physical deterioration and finally dementia and paralysis

Ætiology —Infection with *Treponema pallidum* (*Spirochæta pallida*) is the essen tial cause and the disease usually begins between 8 and 20 years after infection The incidence is much greater among males than among females and the onset of the disease occurs most often between the ages of 30 and 50 It may appear in adolescence as the result of congenital infection The incidence among syphilitics in general has been estimated as high as 5 per cent but among those who have been well treated in the early stages the incidence is probably less than 1 per cent It formerly represented about 10 per cent of all cases of neurosyphilis and nearly a quarter of those treated as hospital in patients

Pathology —At necropsy the brain appears atrophic the sulci being widened and the convolutions reduced in size These changes are most pronounced over the anterior and middle portions of the hemispheres but in some cases only the occipital poles escape The meninges often show considerable thickening and opacity and the pia adheres firmly to the cortex On section the cortex is found to be reduced in thickness The ventricles are enlarged as a result of the atrophy of the brain substance and their ependymal lining appears granular or frosted

The essential changes are in the ganglion cells of the cerebral cortex. Micro scopical examination under the low power shows that many of these cells have dis-appeared and that those remaining are arranged irregularly The cells are often shrunken and their nuclei stain deeply In association with the neuronic damage there is a marked reaction of the glial cells and histiocytes (rod cells) The subpial lamina of glial tissue is increased The histiocytes proliferate and hypertrophy and when stained with Prussian blue are found to contain iron in their cytoplasm—a pathognomonic finding Many of the cortical blood vessels are surrounded by a peri vascular cuff of lymphocytes and plasma cells and the vessels often show prolifera tive changes in their endothelium

Treponema pallidum can be demonstrated in the nervous tissue

Symptoms —For months before intellectual defect becomes apparent the patient has usually shown some defect of emotional control He has become excitable moody liable to outbursts of temper and easily moved to tears by music or the cinema Thereafter he begins to show a lack of concentration and persistence he ceases to pursue his old interests and adopts new ones in rather rapid succession At this

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coma following a fit In some cases convulsions are the first manifestation to attract attention When the patient is examined however it is usually found that he is already tremulous Such cases are among the most favourable for treatment, because the disease may be arrested before mental deterioration has become apparent Insomnia is frequent in the prodromal period but in the early stages sleep is often excessive Later sleeplessness and motor restlessness are often troublesome symptoms

Tabo paresis.—The condition known as tabo paresis consists of a combination of certain features of general paralysis with certain features of tabes The mental symptoms are as a rule relatively mild tremor and the speech disturbances are moderate, the knee jerks and ankle jerks are absent and there is usually some sensory impairment of tabetic type and distribution the pupil reactions are likely to be of the Argyll Robertson type and optic atrophy may be present A considerable number of cases of nervous syphilis in which optic atrophy is the first recognised feature develop as cases of tabo paresis

SEROLOGICAL REACTIONS —Provided the patient has not recently received antisyphilitic treatment his blood will almost certainly give a positive Wassermann reaction A negative result however should not be accepted as conclusive evidence against the presence of general paralysis of the insane The cerebrospinal fluid in an untreated case usually shows an increase in the number of white cells and in the protein content, with excess of globulin, the Wassermann reaction is invariably strongly positive and Lange s colloidal gold test almost always shows maximal changes in the first four or five tubes (paretic type of curve)

Diagnosis —The diagnosis depends on the combination of mental changes with typical changes in the cerebrospinal fluid Tremor is almost invariably present at any rate in the voice In the complete absence of tremor even when the fluid changes are typical it may be doubted whether the condition present is general paralysis of the insane and not one of the other forms of cerebral syphilitic disease Cerebral meningo vascular syphilis may cause mental deterioration and paralysis but tremor is seldom prominent and the changes in the cerebrospinal fluid especially the colloidal gold reaction are likely to be somewhat less intense

In the absence of reliable examination of the cerebrospinal fluid or blood the history of change in the patient s character combined with intellectual deterioration impaired emotional control and tremor is almost sufficient for the diagnosis Commonly the patient himself has little or no insight into his altered state and may express his subjective sense of well being and of intellectual acuity in glowing terms that arouse a suspicion of the true state of affairs in the trained observer The non syphilitic conditions which cause a similar gradual change are rare with the exception of arteriosclerotic dementia The latter usually occurs at a later age than general paralysis and is associated with less tremor In general paralysis pupillary abnormalities are almost constant and slurring articulation soon becomes added to the tremor of the voice

In rare cases chronic alcoholism gives rise to an expansive mental state and tremulousness which cannot with confidence be distinguished from general paralysis without examination of the cerebrospinal fluid With delirium tremens visual hallucinations are a prominent symptom Alzheimer s disease is a rare form of degeneration of the frontal lobes which comes on in middle age and causes gradual mental deterioration associated with tremor Pupillary abnormalities are absent (see p 1630) In the absence of pupillary or other clinical signs of nervous syphilis it may be impossible to distinguish the depressed form of general paralysis of the insane from other states of depression In many cases the tremulousness may suggest the correct diagnosis but some tremor may also be seen in cases of depression with agitation due to other psychoses When a history cannot be obtained and the patient is in a maniacal or a hypomanic state the differentiation from other forms of mania may for a time be impossible

stage he is 'full of ideas' but soon begins to show deficiency of judgment in applying them seeing only the great advantages of his schemes and forgetting his own limitations He assumes his ability to attain every wish, and this may lead to outbursts of wild extravagance By this time he has become forgetful, inattentive to business and careless Within a short time he has actual delusions concerning his own capacity, and he may boast of his physical power, wealth or social position but the classical delusions of grandeur are now a rarity

In many other cases the symptoms are merely those of simple dementia with gradual reduction of interests and of mental and physical activity The patient's ability to perform his usual work is gradually impaired, especially if it is of a mental character, and when calculation is involved his mistakes become frequent In a large number of such cases the patients are depressed in the early stages and the subsequent *delusions may be melancholic or hypochondriacal As the disease progresses,* memory becomes more and more defective excitability and activity give way to apathy and lethargy and delusions die out The patient lies in his bed showing little sign of mental activity indifferent to his surroundings incontinent and more or less paralysed

The first of the physical changes accompanying the mental deterioration is almost always tremor Usually if not always it begins by affecting the voice giving it a vibrant emotional quality but this change usually escapes notice When however the tongue lips and cheeks become tremulous the irregularity of articulation is pronounced The typical tongue tremor is a backward and forward 'trombone' movement of the organ when the attempt is made to protrude it Speech is often affected early At first it is merely hesitant later it becomes indistinct and irregular, syllables are omitted interpolated or slurred and the voice becomes feeble and lacks intonation Utterance then becomes jerky, and consonants are slurred Changes at a higher physiological level in the speech system also occur and cause elision of syllables or of words, and attacks of aphasia are not uncommon As the memory fails confusion arises in the construction of long sentences proper names are forgotten the choice of *adjectives and verbs becomes more and more limited and the* vocabulary diminishes until only interjections are left Written language suffers in the same way and may show defects of execution and of ideation before spoken speech is noticeably altered Tremor becomes marked in the hands and other parts of the body and because of the unsteadiness of the hand the writing deteriorates and with the intellectual deterioration words are often misspelt

Apart from tremor there are no physical signs that can be counted upon in the early stages Pupillary abnormalities are very common but they simply indicate central nervous syphilis and have probably been present for some time before the onset of general paralysis The complete Argyll Robertson phenomenon is not very common but incomplete forms of it and inequality and irregularity of the pupils are usual Signs of disturbance of the pyramidal system—extensor plantar reflexes and exaggeration of the tendon jerks—usually occur before long If any of the tendon jerks are absent as is not uncommon *it is because of the presence of an element* of tabes dorsalis Incontinence of urine often occurs early but it is more often due to lack of attention than to any failure of the sphincter reflexes At a later stage control of both bladder and rectum is always lost. Sexual impotence is present in most cases for several years before mental symptoms appear but in a few of the more acute cases the onset is accompanied or preceded by a phase of sexual excitement

As the disease advances the paralytic features become more pronounced In the so called congestive attacks hemiplegia or monoplegia appears with or without an initial Jacksonian fit Recovery occurs in the course of a few days or weeks but the limbs gradually become weak

Generalised epileptiform seizures are common and often aggravate the pre existing symptoms and in a large proportion of cases death eventually occurs in

more easily controlled methods of producing it were developed, the most successful of which was the heating of the body in a suitable cabinet by electrical short waves

After any successful treatment clinical improvement is very gradual The first clinical effects are the reduction of tremor and of excitability and an improvement in the patient s memory and alertness During the next few months improvement in favourable cases is pronounced but 2 years elapse before the full effect is obtained Changes in the cerebrospinal fluid with one important exception are equally gradual Within a few weeks of the end of successful treatment the number of cells in the cerebrospinal fluid falls to near the normal level (3 per c mm) indicating the cessation of active inflammation in the central nervous system but the other abnormalities in the fluid show for the time being little change The Wassermann reaction of the fluid usually dies out in the course of a year or so but the paretic colloidal gold curve may persist for several years and its presence is not to be regarded as a sign of syphilitic activity If treatment has not been successful in eradicating the infection the first sign of relapse is an increase in the number of cells in the cerebrospinal fluid and such increase will almost invariably be observable by the end of 6 months consequently, if at the end of 6 months the cerebrospinal fluid contains more than four cells per c mm a further course of treatment should be given

The effect of modern therapy is to arrest the active disease and the clinical results depend chiefly on the degree of mental deterioration that had occurred before treatment was instituted The most satisfactory cases are those in which convulsions or other acute phenomena have brought the patient under care before mental impairment has become obvious However, patients with mental symptoms of short duration often do well In cases of slower evolution with evident mental impairment arrest of the disease may leave the patient incapable of useful mental work and unfit to hold any position of responsibility

In occasional cases cerebral degenerative changes of a non specific character occur in later life and give rise to a secondary dementia

CEREBRAL SYPHILIS

Synonym —Cerebral Meningo Vascular Syphilis

Definition —In most of the cases to which the term cerebral syphilis is applied the chief incidence of the syphilitic process is upon the meninges and blood vessels the brain being affected in a less degree and by secondary processes Actual syphilis of the brain is uncommon It occurs however in two forms (1) Gumma of the brain and (2) a diffuse gummatous infiltration throughout the cerebral hemispheres or even in the cerebellum the meninges always being involved to some extent

Ætiology —Cerebral syphilis (as distinct from general paralysis of the insane) occurs in about 4 per cent of all persons who acquire syphilis The onset of symptoms is commonest from 1 to 5 years after infection but it may be as early as 2 or 3 months or as late as 30 or 40 years Characteristically the patients are young men but a stroke due to syphilitic vascular disease may occur at any age and at any interval after infection

Pathology —Both the meninges and the cerebral blood vessels are always affected but the degree of involvement of each is subject to great variation When the disease falls chiefly upon the meninges it most frequently causes a diffuse subacute or chronic gummatous leptomeningitis at the base of the brain Less often it affects the coverings over the convex surface of the brain and if so it is usually more intense over the frontal and parietal lobes than over the occipital and temporal —In severe cases a gelatinous exudate fills the subarachnoid space and extends along the vessels and nerves Later the newly formed tissue organises and forms sclerosed gummata Hydrocephalus

Course and Prognosis—The onset is usually insidious The disease may then progress steadily or in the early stages show exacerbations with maniacal outbursts In the absence of effective treatment death usually occurs within 3 years and in a large proportion of cases the duration is about 1 year If convulsions are frequent the termination is likely to occur sooner and acute cases may run their course in a few weeks Usually the disease is less acute in women than in men

The duration of tabo paresis is generally a good deal longer than that of general paralysis and in cases due to congenital infection the course is often prolonged

Treatment—PROPHYLACTIC—The eventual occurrence of general paralysis of the insane may be feared in any case in which 2 years or more after infection the lymphocytosis in the cerebrospinal fluid is resistant to courses of antisyphilitic treatment Preventive treatment then consists in a course of penicillin injections as in the curative treatment of general paralysis If the interval from the time of infection is as long as 5 years and the colloidal gold curve is of the paretic type, such preventive treatment should not be delayed

CURATIVE—It is important that the physician in charge of a case of general paralysis should have clearly in mind both the possibilities and the limitations of treatment Cure consists of two distinct parts—the eradication of the syphilitic infection from the brain, and the restoration of normal cerebral function The means of treatment at our present disposal may accomplish the former and do not aim beyond that The subsequent restoration of cerebral function depends on the recovery of such cerebral tissue as is capable of recovery and we have as yet no means of influencing the natural course of this process This recovery continues over a period of about 2 years and attains very different degrees according to the amount of damage already suffered by the brain before the disease was arrested the acuteness or chronicity of the inflammation and other factors While the corresponding mental recovery reaches a gratifying level in many patients in whom the disease is recognised and treatment begun reasonably early there are many others in whom it is never sufficient to restore the patient to a position of social usefulness

For the eradication of the syphilitic infection from the brain penicillin now provides the method of choice As however this treatment is relatively new some physicians still prefer to re enforce it with a (shortened) course of pyrexial therapy The penicillin treatment consists of the administration of a minimum of 5 million Oxford units intramuscularly over a period of approximately 10 days and it is now usual to give about 10 million units in a single course or in two courses Having begun with injections of 15 000 units or so three times in the course of the first day it is usual to proceed with doses of the order of 60 000 units every 3 hours until a total of 5 or 6 million units has been attained i e 10 or 12 days more Various methods of maintaining the concentration of penicillin in the blood with less frequent injections, e g one every 24 hours are on trial but none has yet obtained general acceptance No penicillin is given intrathecally During the course of penicillin therapy a mixture containing iodide of potassium (gr 20 or gr 30 to the dose) and mercuric chloride solution (1 in 1000) (½ to 1 drachm in each dose) should be given by mouth with the idea of aiding the absorption of gummatous elements in the brain and meninges

It was discovered in 1917 that general paralysis could be arrested by malaria and for the next 30 years benign tertian malaria was used all over the world as a therapeutic measure The patient was allowed to have from 6 to 12 rigors according to his physical state and then the malaria was stopped by quinine or mepacrine The treatment was mostly carried out in special hospitals or clinics with expert medical nursing staff and under such conditions the mortality (from the disease and from the malaria) during the stage of active treatment was of the order of 10 per cent but under less favourable conditions it was much higher

When it was established that the pyrexia was the actual curative agent various

Fluctuation in the symptoms is one of the features of the disease and in the milder cases the patients may be well for months at a time

Prognosis —With antisyphilitic treatment a large measure of recovery is the rule but some mental impairment headaches and occasional fits are common residual phenomena Signs of hydrocephalus may persist in some degree Hemiplegia may respond to antisyphilitic treatment but in the majority of cases it is little affected

Treatment —Prophylactic —If syphilis has been contracted it should be thoroughly treated in its early stages When the Wassermann reaction of the blood has been rendered negative the test should be repeated once a year for the first 5 years and then every 2 years The cerebrospinal fluid should be examined after the blood has been rendered negative but an interval of 2 or 3 months should be allowed between the end of a course of treatment and the lumbar puncture If the cerebrospinal fluid then gives a positive reaction treatment should be continued and the fluid should be examined as before 3 months after the end of the course of treatment

Curative —As soon as the diagnosis is made and in very acute cases even before it is established antisyphilitic treatment should be begun with potassium iodide and mercury by the mouth and within a day or two a course of penicillin as described for general paralysis of the insane (p 1458) should be started The potassium iodide and mercury can be combined in the following mixture potassium iodide gr 10 to 20 solution of mercuric chloride mins 30 to 60 arsenical solution mins 2½ chloroform water fl oz ½ This should be taken with as much water as desired three times a day after food but is not to be taken when the stomach is empty If either dyspepsia or diarrhœa occurs the mixture should be stopped for a time and replaced by one containing bismuth carbonate gr 15 instead of the solution of mercuric chloride

ACUTE SYPHILITIC MENINGITIS

This is a rare condition almost confined to young men It occurs usually within a year or two of infection and has even been associated with the secondary rash A peculiar feature is that acute syphilitic meningitis or a condition closely resembling it (meningo recidive aigu) may occur during a course of arsenical injections and there is some reason to believe that in such instances the treatment is a precipitating factor

Symptoms —The clinical picture is indistinguishable from that of other kinds of acute meningitis Headache is intense the temperature may rise to 102 or 103 F the patient is delirious and may have maniacal outbursts and stiffness of the neck is present but Kernig s sign is not usually pronounced The optic disks may be blurred and slightly swollen The condition of the pupils is not usually of diagnostic value The tendon and plantar reflexes are variable as in other kinds of acute meningitis The cerebrospinal fluid may contain 1000 or 1500 cells per cubic millimetre of which as many as 30 per cent or even more may be polymorphonuclear The Wassermann reaction is strongly positive both in the cerebrospinal fluid and in the blood

Treatment —With the administration of potassium iodide and mercury by the mouth and the injection of small doses (10 000 to 15 000 units) of penicillin intramuscularly at 6 hourly intervals the fever and delirium quickly subside and the headache abates Treatment must then be pursued on the same lines as for other forms of meningo vascular syphilis Good recovery is the rule but some mental impairment is often left

TABES DORSALIS

Synonym —Locomotor Ataxia

Definition —This is a disease of syphilitic origin characterised clinically by ataxia

may result Many symptoms of cerebral syphilis are caused indirectly and result from hydrocephalus or vascular disturbances In rare instances syphilitic infection gives rise to an acute diffuse meningitis indistinguishable without special tests from other kinds of acute meningitis (see p 1461)

In cases where the main incidence falls upon the blood vessels the arteries at the base of the brain forming the circle of Willis or arising from it, together with their branches are most often attacked To the naked eye they show irregularities in size, due to thickening of their walls in circumscribed areas Proliferation of the intima, together with a round celled infiltration of the outer coats—endarteritis obliterans—is the characteristic microscopical change In smaller arteries within the brain or on its surface the same changes occur and these vessels as well as those at the base may be compressed or invaded by disease beginning in the meninges In each case their lumen is narrowed or obliterated thrombosis occurs readily and softening results in parts from which the blood supply is cut off Obliterative changes also occur in the veins and perivascular spaces and lead to further impairment of the nutrition of the brain

Gumma of the brain is rare When present it arises from the meninges and may be multiple and the convexity of the hemisphere in the motor region is the site of election A gumma may spread so as to involve the overlying bone

Symptoms —The symptoms of basal meningitis are partly general and partly local from involvement of some of the cranial nerves The general symptoms are headache, lethargy and impairment of intellect and memory The headache is deep seated and severe The lethargy is variable and may pass off for a time or may deepen into stupor Any one or several of the cranial nerves may be paralysed Ocular symptoms are rarely absent pupillary changes being the rule and external ocular palsies common Mild papillœdema is also common and optic atrophy may occur in one or both eyes A symptom presumably due to involvement of the hypothalamus or of the pituitary is obesity Diabetes insipidus sometimes occurs

When the meningitis is distributed chiefly over the convexity of the cerebral hemispheres there may be long periods of intermittent headache which is acute and usually situated near the vertex of the skull and the skull may be tender In severe cases convulsions are common they are most frequently generalised epileptiform fits but Jacksonian attacks are not uncommon and are usual in the more chronic cases Attacks of aphasia may occur In all the more severe cases some mental impairment is the rule usually simple dementia but there may be mild delusions and emotional instability is common

When the blood vessels are predominantly affected premonitory symptoms often occur before there is any severe stroke These consist of transitory weakness of one arm or other part of the body or of local twitching Headaches are common Hemiplegia is the usual syndrome which supervenes and in some of these cases it is of the most severe type In addition to the paralysis and spasticity there may be sensory loss in the affected limbs and complete or partial hemianopia Aphasia usually accompanies right sided hemiplegia The Wassermann reaction is usually strongly positive in the blood

Diagnosis —This depends largely on the discovery of a positive Wassermann reaction It is usually positive in the blood but in many cases it is negative in the cerebrospinal fluid Pupillary abnormalities may be of great help in suggesting syphilis as a cause but the possibility of a tumour in the mid brain must be borne in mind The Argyll Robertson pupil in its pure form is not common in cerebral meningo vascular syphilis

Jacksonian epilepsy or fits of any kind in patients—particularly male patients between 21 and 25—are suggestive of syphilitic meningitis or gumma even though these are not now the commonest cause of such symptoms This applies particularly if the attacks are of a peculiar character such as an attack of automatism and amnesia

several years' duration In other cases the patient mentions his pains but their significance escapes notice because it is thought that they are too slight to be tabetic pains It must be made clear at once therefore that the peculiarity of the pains in tabes does not lie in their severity for they vary from a trifling sensation of discomfort to almost intolerable agony, but in their distribution, in their direction of propagation, and especially in their arrangement in time

As a rule they come on in attacks in which single momentary pains are repeated at intervals of a few seconds or minutes for several hours the whole bout lasting several days or weeks Between the attacks there may be long intervals of complete freedom from pain The pains are felt most often in the lower limbs but any part may be affected They may be referred to the skin to the muscles or to the bones They are very common in the bony prominences around the knee and on the foot. The direction of radiation varies In some the pain seems to shoot up or down a limb but in a larger number it seems to strike the limb vertically, as if a sharp object were piercing it from without. Some patients experience both kinds of pains The onset of each pain is always sudden If it is severe the patient may cry out and if it overtakes him whilst walking he is forced to stop The duration of each pain is usually momentary, but sometimes it lasts a second or two and fades away gradually

Other pains with characters which are not peculiar to tabes are common They are described as aching burning or gnawing pains Like the lightning pains they alter with changes in the weather and are usually attributed to rheumatism Other common subjective sensory symptoms are pins and needles in the extremities a feeling of walking on a soft substance and of constriction around the trunk or limbs. More important than these because it often appears very early is hyperæsthesia of the trunk, especially in its lower part Light touches or applications of water at certain temperatures are almost unbearable In cervical tabes sensory disturbances occur first in and are more severe in the arms

Objective—In association with the foregoing subjective disturbances objective impairment of pain appreciation develops For some unknown reason this impairment (hypalgesia) has a strongly selective incidence the areas at first affected being as follows (i) a band across the chest, (ii) over the lower halves of the shins (iii) on the nose and (iv) on the ulnar borders of the forearms As the disease advances the areas thus affected extend and eventually pain appreciation may be impaired over the whole surface of the body Deep pain appreciation becomes similarly affected

REFLEXES —Simultaneously with the involvement of the pain fibres, or very soon afterwards the fibres which subserve reflex activities are affected with consequent gradual interruption of the reflex arcs The ankle-jerks and knee-jerks disappear. Loss of the ankle-jerks is an early sign in tabes, and often precedes loss of the knee jerks by many years The tendon reflexes in the upper limbs are lost early in cervical tabes and are frequently absent in cases of the ordinary type The triceps-jerk is usually the first to go. The skin-reflexes are often exaggerated to a degree rarely met with in other diseases This is best seen on the abdomen and is usually associated with hyperæsthesia to touch and temperature The plantar reflex is usually normal It is sometimes absent when sensory loss on the soles is severe and in cases where sclerosis of the pyramidal tract exists as a complication of tabes the response is extensor

HYPOTONIA —Muscle tone which is a reflex function gradually becomes affected too and in any established case passive movement of the lower limbs reveals definite hypotonia The decrease in the tone of the muscles is often well marked at a time when lightning pains are the only symptom of tabes and loss of skin sensation the only other manifestation It is shown by flaccidity of the muscles, and by an abnormal range of active and passive movement of the limbs. The leg can often be raised to an angle of 100 from the horizontal with the knee extended whereas a normal

of the lower limbs in walking and by numerous other signs and pathologically by degeneration of the posterior columns of the spinal cord

Ætiology —Syphilis is the essential factor in causation Little is known of the contributory factors which determine the occurrence of tabes dorsalis in some persons with syphilis and not in others Males are affected a good deal more frequently than females The onset is usually between the ages of 30 and 45 years and usually between 5 and 15 years after infection It may occur in both husband and wife—"conjugal tabes" It also occurs not very rarely as a result of congenital syphilis and then appears in adolescence or early adult life

Tabes dorsalis was once the commonest form of neurosyphilis but its frequence has shown a marked decline in recent years

Pathology —The most evident morbid change is degeneration in the posterior columns of the spinal cord It is however generally believed that this is not primary but results from disease affecting the fibres of which these columns are composed before they enter the cord These fibres and other fibres of the posterior spinal roots are most probably affected by syphilitic toxins either where the nerves pass through the meninges or where the roots enter the spinal cord As a secondary change the neuroglia around the degenerated fibres increases in amount and density Hence the characteristic feature in sections of the cord in tabes is shrinkage and sclerosis of the posterior columns The sclerosis usually appears earliest in the postero lateral columns of the lower lumbar and upper sacral regions but in advanced cases when the dorsal and cervical sensory roots are also affected the posterior columns are sclerosed through out In advanced cases the endogenous tracts of the posterior columns show degeneration, and in some the afferent tracts in the lateral columns are also affected In addition there is often a subpial or marginal degeneration practically all round the cord at many levels

Atrophy of the optic nerves commonly occurs and seems to be the result of a combined interstitial gummatous inflammation and primary degeneration of the nerve fibres The ocular palsies of tabes are probably mainly due to gummatous meningitis but there may be a degeneration of the nerve cells in the nucleus of the third nerve

Symptoms —Few diseases cause so many different symptoms The most common features are (i) lightning pains , (ii) objective disturbances of sensation (iii) loss of tendon reflexes (iv) ataxia (v) disturbance of pupillary reflexes especially the Argyll Robertson pupil and (vi) impairment of bladder control Less frequent are (vii) visceral crises', *i e* acute disturbances of function of certain viscera of which gastric crises are the most common but rectal vesical and laryngeal crises also occur (viii) atrophy of the optic nerves (ix) trophic changes—(*a*) Charcot s disease of joints (*b*) perforating ulcers of the skin and (*c*) a general trophic effect which renders the patients thin

The usual syndrome is essentially that of degeneration of the posterior spinal nerve roots, or of the corresponding nerve cells in the posterior root ganglia and, in fact of the afferent elements of the nervous system in many parts of the body

SENSORY DISTURBANCES —*Subjective* —Lightning pains are usually the first symptom—sudden intense stabbing pains which seem to shoot into parts of the lower limbs They occur at irregular intervals and usually in bouts vary greatly in severity, and are often mistaken for rheumatism or neuritis These pains merit the closest attention They are rarely absent they often precede other symptoms by 5 or 10 or more years and most important of all they possess peculiar features which render them pathognomonic of tabes and allow the diagnosis to be made in a syphilitic subject on their presence alone Although they are rarely absent careful interrogation may be needed to disclose them To the question Have you any pains ? the patient may answer No If then he is asked if he has rheumatism he will often answer Yes and proceed to give an account of characteristic tabetic pains of

comes on at a later stage and it is compensated for by elevation of the eyebrows In addition there are a general flabbiness of the facial musculature and a greyish pallor of the skin All these features combine to give the patient a somewhat distinctive facial appearance—the tabetic facies

Optic atrophy.—Syphilitic optic atrophy is an important complication and occurs with such frequency that it is often called tabetic optic atrophy It has been estimated that it is found in about one case in ten It may be the first indication of neuro syphilis The peripheral portion of the visual field is lost first, and charts of the fields at this stage have a most irregular outline Central vision is the last to fail and as long as it persists the impairment of sight may escape notice The most acute cases proceed to complete blindness in 2 months but the slow cases take many years or remain unilateral The atrophy is primary, that is it is not preceded by papill œdema The disk becomes white and flat, and is sharply outlined. Cases of tabes which begin with optic atrophy do not, as a rule, develop much ataxia, but they often develop mental disturbances and become cases of tabo-paresis

VISCERAL CRISES —Occasionally attacks of intractable vomiting occur each lasting a few days and during this time the patient cannot keep anything down The vomiting may be associated with epigastric pain but more often there is merely discomfort. Tabetic pains in the back are commonly associated with or precede the crisis When the attack is over the patient is quickly well again, but such attacks continue to occur at intervals of months or weeks They often take place before other symptoms of tabes dorsalis have attracted attention, and the vomiting is not infrequently attributed to intestinal obstruction or to perforation of the stomach with the result that laparotomy is performed Rectal crises consist of painful and prolonged tenesmus, vesical crises of severe dysuria and laryngeal crises of prolonged spasm of the larynx causing stridor cough and dyspnœa

TROPHIC CHANGES —*Charcot s disease of joints*—In some cases, usually those of a very chronic type severe disease leading eventually to articular disorganisation occurs in one or two joints The first sign is usually rapid swelling in and around a joint, with effusion and œdema The effusion in slight cases subsides slowly and the joint recovers but more often the enlargement is followed by destruction of the cartilages wasting of the ends of the bones periarticular new bone formation and destruction of the ligaments The joint becomes disorganised, the range of movement is increased and crepitations of startling coarseness are heard and felt when the part is handled The characteristic feature is the complete absence of pain Dislocations occur readily especially at the hip and the presence of an arthropathy may be first revealed by the occurrence of a pathological fracture of the neck of the femur The diseased joint sometimes becomes infected most frequently in the foot The joints most often attacked and in order of frequency are knee hip ankle, small joints of the hands and feet the spine shoulder and elbow

Charcot s disease of joints is very frequently associated with negative Wassermann reactions both in the blood and the cerebrospinal fluid In one instance in which the blood and cerebrospinal fluid gave negative results fluid aspirated from the affected joint gave a strongly positive reaction

In certain tabetic patients changes occur in some of the bones so that they break with a small degree of violence

Perforating ulcers of the skin—Trophic changes in the skin give rise to chronic ulcers, usually on the sole of the foot which gradually increase in depth until the foot may be perforated These ulcers like the other trophic disturbances of tabes are usually painless

Tabetics tend to get thin and a slow loss of weight is an early sign If there is any tendency for the weight to increase a paretic element is almost certainly present. Manifestations of syphilis in other organs are rare in the course of the disease with the exception of aortitis, which occasionally occurs

person cannot raise it more than 60°, and excessive range of *dorsiflexion of the foot* is often a striking sign In extreme cases the legs can be made to encircle the neck the body can be flexed so that the head touches the bed between the knees and the patient is able to imitate the tricks of the double jointed man

ATAXIA —At a slightly later stage the coarser fibres in the posterior roots which are concerned with sense of position suffer in the same way as the pain and reflex fibres The patient then becomes unable to appreciate exactly the position of his extremities As a rule the lower limbs are affected first and most The patient becomes unable to direct the movements of his feet exactly and fails to maintain his centre of gravity in the right position relative to them with the result that he becomes unsteady The trouble is first noticed when co ordinated movements have to be performed without the aid of vision, as when the patient is washing his face in the morning This disability is partly overcome for a time by separating the feet so that the patient stands and walks on a wide base, he watches the ground and is much more unsteady with his eyes closed or in the dark When standing with his feet together he is more unsteady with his eyes closed than with his eyes open (Romberg's sign) As the loss of sense of position advances and at the same time the controlling influence of muscle tone is lost movements of the lower limbs become very irregular In walking the feet are raised too high and are brought down with irregular force often too violently so that the gait becomes stamping The steps are of irregular length The patient staggers from side to side and may fall Eventually walking may become impossible The same inco ordination of movement occurs in the upper limbs but usually in less degree The patient becomes unable to direct the movement of his hands and fingers exactly without watching them later he becomes clumsy and eventually may become unable to feed himself

SPHINCTER TROUBLES —These are the result of lowering of pain sensibility in the bladder which is the afferent element in the reflex of micturition An increased distension of the bladder becomes essential before the act can be started and this fails before the bladder is completely emptied and residual urine is present in slowly increasing quantity Though this causes little or no inconvenience to the patient at first it often leads to cystitis and renal complications Later, difficulty in starting micturition and nocturnal incontinence are common Acute retention of urine is sometimes the symptom which first brings the patient under observation but retention at any stage of the disease may be attributable to enlargement of the prostate, and removal of the latter may give complete relief Sexual desire and power are usually lost early in the course of the disease

OCULAR DISTURBANCES —While manifestations referable to spinal root disturbances are developing certain others arise in the areas supplied by the cranial nerves The most important are abnormalities in the reactions size and outline of the pupils and pupillary disturbances of some kind are often the first signs of the malady The Argyll Robertson pupil is the most characteristic abnormality *but it is not common* in its pure form namely, a very small pupil which reacts *normally to convergence* but *not at all to* light, and does *not dilate fully under the influence of a mydriatic* (see p 1343 1466) Absence *of the light*-reaction in one or both pupils with or *without retention* of the convergence reaction is usual and atrophic changes in the irides are very common

The size of the pupils varies greatly in different cases Most often they are small, but pupils of moderate size are common and sometimes they are widely dilated though this is very exceptional and is usually associated with optic atrophy *It is* not unusual to see pupils which when contracted to accommodation are *not much* larger than the head of a pin but the pin-point pupils are rare *Inequality of the pupils or irregularity in their outline is present in most* cases In old tabetics in whom the disease has been *present for very many* years the pupils may be found *wholly inactive* both *to light and* on convergence Partial bilateral ptosis usually

it is usually impossible to determine the sequence and duration of the signs that are found but if the onset of lightning pains and of ataxia are taken as landmarks an idea of the extreme variability of the course of tabes in different cases will be obtained In many patients the disease remains stationary in an early stage and causes no disability In a larger number however, inco-ordination appears after a pre ataxic stage of 10 or 20 years Some become ataxic within 5 years of the onset of pains a few within a year Once ataxia appears its rate of increase varies within wide limits It may be so rapid that walking becomes impossible in a few weeks it often increases very slowly, and only interferes seriously with walking after several years while in a large number periods of increase alternate with long periods in which the symptom is either stationary or undergoes temporary amelioration

The course of the other symptoms is equally variable In general irritative phenomenon—pains and crises—tend to diminish while the manifestations of destruction of afferent fibres—diminished sensation hypotonia etc.—increase Ocular palsies are frequently of short duration and bladder and rectal symptoms are often temporary It is impossible to foretell how any given case will progress but there seems to be some connection between the period which has elapsed since syphilis was contracted and the rate of evolution of the disease—the longer the former the more benign the course If the symptoms have increased slowly in the past the future course is likely to be slow whereas cases of rapid onset often progress rapidly When optic atrophy occurs blindness usually results eventually and a proportion of these cases develop general paralysis of the insane

The prognosis as to life is variable. Most tabetics die of intercurrent maladies, or of some cardio-vascular complication In many cases as the result of efficient treatment, the malady undergoes arrest and the patient may never become ataxic or grossly disabled Such arrest may also be found in benign cases in persons who have at no time had any antisyphilitic treatment Conversely treatment is not always successful and tabetics who have been rigorously treated may become progressively disabled On the whole the prognosis as to both working capacity and life is best in those cases in which the bladder can be kept free from infection

Treatment.—PROPHYLACTIC —This is on exactly the same lines as the preventive treatment of neurosyphilis in general The diminution in the incidence of tabes dorsalis suggests that the present methods of treating syphilis in its early stages are much more effective in preventing tabes dorsalis than in preventing other forms of neurosyphilis

SPECIFIC —When tabes dorsalis is associated with a positive Wassermann reaction in the blood or in the cerebrospinal fluid the specific treatment is the same as that described for general paralysis Pyrexial treatment by short wave therapy (but not by malaria) may occasionally be advisable either because of persistent severe lightning pains or of abnormalities in the cerebrospinal fluid which are not abolished by repeated courses of penicillin.

When the Wassermann reaction is negative in the blood and cerebrospinal fluid it is sometimes difficult to judge how much antisyphilitic treatment should be given and the decision must depend on the clinical indications of activity of the disease Lightning pains show that the disease is active Even after all clinical evidence of activity has ceased it is well to give the patient three or four times a year a month s course of a mixture of potassium iodide and liquor hydrarg perchlor

TREATMENT OF SYMPTOMS —*Pains* —These may be relieved with aspirin and other analgesic drugs Morphine should not be employed A course of antisyphilitic treatment usually reduces or stops the pains for a long time Exposure to cold sometimes seems to precipitate or aggravate pains and should be avoided as far as possible In severe and intractable cases the operation of spino thalamic cordotomy is justified

Ataxia —This can be greatly diminished in many patients by a course of Frenkel s exercises Just as a normal person by practice and effort can learn to perform feats

Diagnosis —Tabes dorsalis is diagnosed by its clinical features Examination of the blood and cerebrospinal fluid may not provide any evidence of syphilis, the Wassermann reaction is negative in one or the other in about 30 per cent of cases and completely negative in both in about 15 per cent. The diagnosis rests on (1) lightning pains, (2) characteristic sensory signs, (3) the Argyll Robertson pupil in one or both eyes (4) absence of one or both ankle or knee jerks, or a definite *diminution* in one of them and (5) evidence of syphilis.

Patients rarely seek advice until the clinical manifestations are fairly well established unless their early pains are severe or gastric crises occur Even then it is nearly always found that the pupils are abnormal, the ankle jerks are absent and hypalgesia is present over some of the characteristic areas The knee jerks may still be present and even normal, but this should not interfere with the diagnosis if the ankle-jerks are absent

Disseminated sclerosis often causes ataxia in the gait and may even in rare instances cause absence of the ankle-jerks, but signs of involvement of the pyramidal tract are usually definite the light reflex of the pupil is retained, and superficial sensory loss if any has not the distribution and the selective character that are typical of tabes dorsalis

Friedreich's ataxia is distinguished from tabes by the presence of pyramidal tract signs, dysarthria, nystagmus pes cavus and usually some degree of scoliosis Juvenile tabes is the most likely to be mistaken for Friedreich's disease

The effects of cerebellar ataxia are usually pronounced in the upper limbs and in the articulation as well as in the gait the pupils are not affected, the tendon jerks though possibly diminished are not absent and there is no sensory loss and no sphincter disturbance Because of these features the differential diagnosis from tabes is usually easy

Peripheral neuritis causes loss of tendon jerks and diminished sensation over the peripheral parts of the limbs, and frequently causes ataxia but there is usually also a loss of power in the extremities and possibly wasting there is no sensory loss on the chest and nose the pupils are not affected and in many cases the calves are very tender instead of being insensitive to pressure as they are in tabes

Subacute combined degeneration of the cord associated with pernicious anæmia gives rise to ataxia, and loss of the ankle jerks and knee jerks, but the plantar reflexes are extensor, and the blood picture is that of pernicious anæmia although the anæmia *may not be pronounced*

There are two groups of cases between which the diagnosis is especially difficult and in an individual case may be impossible On the one hand there is a group of cases of mild tabes occurring in adults but due to congenital infection in which the blood Wassermann reaction is negative and the cerebrospinal fluid is completely normal and on the other the group of non syphilitic cases described by Foster-Moore and by Adie in which the patients have ' tonic ' or ' pseudo-Argyll Robertson ' pupils and absent tendon jerks (see p 1344) In the former group the typical patient is undersized and of poor physique He comes under observation as a rule for some symptom which is not tabetic fits being a frequent presenting feature one or both pupils may be of true Argyll Robertson type and probably irregular in outline and lightning pains mild bladder trouble or some other feature of tabes may be present A family history of syphilis may be obtained The typical patient in the other group is of normal physical development The pupillary abnormality is probably limited to one eye and the patient may be able to give a history of its onset The irides look healthy Apart from the abnormal pupil and some absent tendon jerks the patient presents none of the multitudinous signs of tabes and there is no history of syphilis in the family or in the individual.

Course and Prognosis —In most instances tabes dorsalis is well established before some serious symptom brings the patient under observation. For this reason

it is usually impossible to determine the sequence and duration of the signs that are found but if the onset of lightning pains and of ataxia are taken as landmarks an idea of the extreme variability of the course of tabes in different cases will be obtained In many patients the disease remains stationary in an early stage and causes no disability In a larger number however inco-ordination appears after a pre ataxic stage of 10 or 20 years Some become ataxic within 5 years of the onset of pains a few within a year Once ataxia appears its rate of increase varies within wide limits It may be so rapid that walking becomes impossible in a few weeks it often increases very slowly and only interferes seriously with walking after several years while in a large number periods of increase alternate with long periods in which the symptom is either stationary or undergoes temporary amelioration

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of balance and muscular co ordination which are impossible for one untrained so the tabetic by concentrating his attention on his movements can be taught to make greater use of his remaining powers and the results of re educative treatment are often astonishing In the more severe cases and when the patient is confined to bed, Frenkel s bed exercises should be employed Constant supervision of the re educative exercises is essential and the treatment should begin in an institution or under the supervision of a skilled attendant

Bladder disturbances—When there is any difficulty in passing water a mixture containing 5 minims of liq strychnine thrice daily will be found useful When the bladder is imperfectly emptied the use of the catheter should not be delayed Only too often neglect of this matter leads to death from pyelo nephritis It is well to re member that serious infections may run a painless course and their presence must be sought for even when pain is absent This entails an examination of the urine from time to time for evidence of inflammation in the urinary tract If pus cells are present in the urine chemotherapy should be tried and if this is unsuccessful the bladder should be irrigated daily until the urine becomes normal True incontinence of urine is often diminished by 5 minim doses of tincture of belladonna thrice daily or by the use of the following pill ℞ Ergotin (Bonjean) gr 1 Ext Belladonn gr ¼ Ft Pil Sig 1 t d s p c

Crises—Gastric crises, like the pains, are very resistant to treatment The follow ing should be tried Tinch chlor et morph co min 10 to 15 bismuth carb gr 15 Ac hydrocyan dil min 5 aq ad fl oz ½ Ft mist sig One tablespoonful to be taken in water every 3 or 4 hours Ephedrine, gr. ¼ or gr. 1 may also afford relief and may be given alternately with the mixture The use of morphine is not justified Rectal crises are sometimes relieved by small doses of grey powder with opium or pulv ipecac et opii The lower bowel should be emptied daily by enemata In mild cases with morning diarrhœa an enema or a suppository should be used before the first evacuation Thereafter the patient should try to resist the desire to defæcate which soon passes away and with a little training this troublesome symptom can usually be overcome Laryngeal crises, though very alarming are practically never fatal They are usually relieved at once by an inhalation of nitrite of amyl.

Optic atrophy—As soon as syphilitic optic atrophy is recognised energetic anti syphilitic treatment is urgently called for and for this condition particularly the use of penicillin has largely superseded other measures No time should be lost in instituting penicillin therapy but it should be started cautiously with doses of 10 000 to 15 000 units at 6 hourly intervals during the first day and unless the case is an acute one should be preceded for a day or two by the administration of potassium iodide and mercury by mouth, as described for general paralysis of the insane The dosage of penicillin should be increased rapidly to at least half a million units daily and a total of 10 million units should be given mercury and potassium iodide being continued meanwhile and for some weeks afterwards In acute cases and especially when one eye is already blind sympathectomy by excision of the stellate ganglion has been used for the purpose of increasing the circulation to the optic nerve on the better side Previously malarial treatment was commonly used and some authorities still prefer to use this or some other pyrexial treatment as well as penicillin but it is doubtful whether this is of additional benefit and the results obtained by various observers with penicillin alone are much better than those which preceded the intro duction of this remedy

After such a course of treatment the deterioration of vision is usually retarded and in favourable cases is arrested but the patient must be kept under close super- vision and any exacerbation of his visual symptoms should be regarded as a call for further treatment on the same lines as before If the Wassermann reaction remains positive in the blood the older antisyphilitic remedies may be employed but arsen icals should be used judiciously and doses of 0 6 g of neoarsphenamine should not

be exceeded tryparsamide should not be given because of its toxic effect on the optic nerve fibres

Charcot's joints —As soon as this condition is discovered the patient should be put to rest the joint immobilised and those measures used which tend to relieve the œdema and the effusion into the joint, and if occasion demands the joint should be aspirated When the joint becomes dry it should be rested for a long period Arthrodesis is the most satisfactory treatment for the knee joint In the case of the hip joint a satisfactory result is obtained with a caliper

Perforating ulcers —These should be curetted and dressed with a paste of iodine and starch

OTHER FORMS OF SPINAL SYPHILIS

ACUTE TRANSVERSE MYELITIS

This condition is now fortunately rare in England The patients are almost invariably males between the ages of 30 and 45 and the malady usually arises within a few years of infection but it may come on at any time

Over one or two segments of the spinal cord there is intense infiltration with small round cells and red cells and there may be small areas of softening The surrounding meninges show similar local infiltration

The symptoms are identical with those of acute transverse myelitis due to other causes (see p 1542) and the ætiological diagnosis depends on the discovery of evidence of syphilis As the onset is usually within a few years of the first infection the pupils are usually normal or not affected in any characteristic way a history of syphilis is often obtainable the Wassermann reaction is positive in the blood or cerebro spinal fluid and usually in both

Treatment with penicillin should be instituted carefully in all cases without waiting for the results of laboratory tests and when the presence of syphilis is con firmed it is probably helpful to add mercury and potassium iodide to the treatment (see p 1461) A course of ten million units of penicillin is sufficient to eliminate the infection but much of the damage to the spinal cord is of a permanent nature

The first sign of recovery is usually some return to muscular tone in the lower limbs and this is followed by the development of extensor plantar and of withdrawal reflexes Recovery of power and sensation continues slowly over many months but usually remains very incomplete

ERB'S SYPHILITIC SPASTIC PARAPLEGIA

This is a slowly developing condition which comes on many years after syphilitic infection The spinal cord shows degeneration of the pyramidal tracts and some marginal degeneration involving particularly the direct cerebellar tracts

Spasticity of the lower limbs becomes pronounced with corresponding weakness and typical reflex abnormalities Sensory changes if any are slight but vesical disturbances are the rule Pupillary abnormalities may or may not be present

PACHYMENINGITIS HYPERTROPHICA CERVICALIS

In rare cases the dura mater in the cervical region undergoes a great gummatous and subsequently fibrous thickening and the arachnoid and pia also become thick ened and fused with it The new tissue compresses the nerve roots and weakness wasting and sensory loss gradually develop in the arms After a time the spinal cord is compressed and spastic paraplegia results

SYPHILITIC AMYOTROPHY

This closely resembles idiopathic progressive muscular atrophy (see Progressive Muscular Atrophy p 1554)

The spinal cord shows degeneration of the anterior horn cells, most pronounced in the cervical region, and also some syphilitic changes in the meninges and blood vessels

The pupillary changes suggestive of neurosyphilis are absent in most of the cases The muscular atrophy usually begins in the upper limbs, and, as a rule, the tendon jerks in the affected limbs are absent, the lower limbs may be normal, or may become spastic or show wasting or may merely lose their tendon jerks but in some cases the wasting muscles retain their tendon jerks Not infrequently there is some sensory loss of the tabetic type, and vesical disturbances are common.

The course may be steadily progressive, but in recent cases it is usually arrested by antisyphilitic treatment In others the condition may remain stationary for long periods

Treatment —*For all kinds of spinal syphilis* the antisyphilitic treatment is the same as that described for general paralysis of the insane and it should be controlled in the same way by examination of the cerebrospinal fluid

SUBACUTE AND CHRONIC SYPHILITIC MYELITIS

Synonym —Subacute and Chronic Spinal Syphilis

Ætiology —The less acute forms may appear within the same age period and at the same interval after infection as the more acute, but on the whole they appear later

Pathology —The meninges become adherent and considerably thickened They are infiltrated with small round cells especially round their vessels Similar infiltration is found round the vessels in the cord and along the septa Changes in the nervous elements in the cord are usually limited to degeneration of fibres round the periphery

Symptoms —After a period of pain in the back lasting weeks or months, there is a gradual development of spastic paraplegia The latter may at first be variable In most cases bladder control is impaired and this may be the first symptom There are usually some objective sensory disturbances in the lower limbs but they are generally slight in comparison with the motor disturbances and may involve only certain qualities of sensation *e g* appreciation of temperature or of vibration or sense of position in the toes Evidence of tabes dorsalis may be present in which case the knee jerks and ankle jerks may be absent, and the degree of spasticity is likely to be slight

Syphilitic meningitis may affect the cauda equina In that event it gives rise to a flaccid weakness of the parts below the knees and weakness or paralysis of the vesical and anal sphincters. Some sensory loss may be found over the characteristic area on the buttocks and perineum

Diagnosis —In the cases which occur within 5 years or so of infection the Wassermann reaction will almost certainly be positive in the blood or in the cerebrospinal fluid or in both In those which develop many years after infection the Wassermann reactions may be negative Pupillary abnormalities suggestive of neurosyphilis and sensory loss of the tabetic type on the chest arms and nose are likely to be present

Course and Prognosis —The former is very variable Some cases show considerable remissions and aggravations others a fairly steady deterioration The rate of increase of paralysis may be very slow or may lead to complete incapacity in a few weeks or months Eventually urinary infection and bed sores may develop

Antisyphilitic measures arrest the disease and usually bring about a fair degree of recovery

Treatment—This is the same as for other forms of spinal syphilis together with special precautions for the bladder weakness (see under Tabes) and symptomatic treatment of the paraplegia

SPINAL VASCULAR SYPHILIS

In rare cases the symptoms indicate that the chief incidence of the syphilitic disease is on the blood vessels of the spinal cord (see also Acute Syphilitic Transverse Myelitis on p 1469)

Thrombosis of a segmental branch of the anterior spinal artery gives rise to sudden paralysis of the muscles of one side deriving their nerve supply from the same segment of the cord *e g* paralysis of the deltoid and scapular muscles and weakness of the triceps brachii muscle when the fifth cervical segment is affected Similar paralysis in the opposite corresponding limb may occur within a few days If the main anterior spinal artery becomes thrombosed in the cervical region there is complete paralysis of both upper limbs with the exception of the hands Either at once or within a few days sensory loss to pain and temperature appears in the arms The muscles waste and the clinical picture resembles that of syringomyelia The tracts of the cord are little affected and abnormal signs in the lower limbs are absent or slight The Wassermann reaction is likely to be strongly positive in the blood but may be negative in the cerebrospinal fluid

At necropsy softening or cavitation within the cervical enlargement is found

The treatment is the same as that of other forms of meningo vascular syphilis

CONGENITAL SYPHILIS OF THE NERVOUS SYSTEM

Affections of the nervous system are much less frequent in congenital syphilis than in the acquired disease Viewed broadly the pathological changes and the clinical manifestations are the same in both Regarding the first meningitis endarteritis and gummata are common to both forms but while *softening* from arterial disease is characteristic of acquired syphilis *cortical cell atrophy and subsequent sclerosis* are prominent features in congenital cases As for the symptoms mental defects with convulsions and spastic weakness of the limbs, are typical of congenital syphilis in contrast to the hemiplegias and monoplegias with or without convulsions which occur in the acquired form It is noteworthy that the combination of obvious visceral and integumental lesions with parenchymatous degeneration of the nervous tissue, is very common in the congenital but not in the acquired disease

Symptoms—Many syphilitic infants suffer from convulsions during the first 2 years of life and in many cases these are given as the cause of death In those who survive fits may continue or they may begin again towards the end of childhood the latter being more common The fits in some cases have all the aspects of idiopathic epilepsy and may continue throughout life without the addition of any symptoms suggestive of local brain disease In another group convulsions are followed by symptoms of hemiplegia or of spastic diplegia, The same defects may appear apart from convulsions Hydrocephalus develops in some cases

Mental impairment is one of the common features of the disease Idiocy is rare More often the defect is first noticed between the ages of 5 and 15 years The child may merely cease to learn and retain any acquirements he possesses or he may lose his memory and become slowly demented

Vision is often defective as a sequel of atrophy of the optic nerve or of choroidoretinitis or simply of interstitial keratitis, and bilateral deafness is not uncommon Affections of the remaining cranial nerves are rare

Juvenile general paralysis appears most often between the ages of 10 and 17 years It has been seen as early as the eighth and as late as the thirtieth year In some cases it results from congenital syphilis in others from syphilis acquired in infancy or in childhood The physical signs are the same as in the adult form The mental symptoms as might be expected, differ from those in adults when mental decay sets in before the appearance of the instincts and passions which form the content of the delusions in older patients A boy of 12 for example is not likely to have delusions regarding his wealth or his intellectual capacity or his sexual powers although he may well have grandiose ideas concerning his physical strength Optic atrophy is very common in juvenile cases and as in adults, signs of tabes are present in many cases

Juvenile tabes presents the same features as in adults It is however, very uncommon in its pure form because most cases begin with optic atrophy and go on to tabo paresis It is important to remember that in rare instances tabes in an adult owes its origin to congenital syphilis or to syphilis acquired in infancy In such cases the blood and cerebrospinal fluid are usually normal

The diagnosis of congenital syphilis of the nervous system rarely causes any difficulty, as the patients almost invariably present some of the stigmata of their malady

One or more courses of penicillin should be given until the cell content of the cerebrospinal fluid becomes and remains normal and thereafter treatment by mercury should be carried on but the results are often disappointing

THE DEMYELINATING DISEASES

DISSEMINATED SCLEROSIS

Synonyms —Multiple Sclerosis, Insular Sclerosis

Ætiology —After intracranial new growths and cerebral vascular disease disseminated sclerosis is probably the commonest incapacitating disease of the nervous system having displaced in this country at least, syphilis of the nervous system It has its highest incidence in northern Europe, is less common in North America and relatively rare among the white population of the Southern hemisphere

Cases have been recorded in which the disease was first noticed after acute illnesses such as scarlet fever influenza and rheumatism but it is probable that these simply made more prominent a condition already present Febrile illnesses are usually followed by increase in the symptoms and many patients with disseminated sclerosis relate that they became much worse after an attack of influenza In the great majority of the cases there is nothing in the family or personal history to which the disease can be attributed In one instance confirmed by examination after death it attacked a mother and her child and a few similar cases as well as the affection of several members of a family or of a household have been recorded

The onset is most frequent between the ages of 16 and 30 the sexes being affected equally It is rare for the disease to begin after the age of 55

The cause is still wholly unknown There is no sure evidence that any of the demyelinating diseases of the nervous system are directly due to the action of a filtrable virus The signs of inflammatory reaction in this disease are compatible with the view that it is infective in origin but it may be added that it behaves like no known infective disease

Pathology —The disease has been described by Nageotte and Riche as an affection constituted by multiple inflammatory foci varying greatly in size and

number disseminated irregularly throughout the length of the cerebrospinal axis The chief features of these foci are (i) their sharp outline (ii) their irregular and capricious shape (iii) the fact that they do not interrupt the axis cylinders which are only demyelinated and deformed as they traverse the focus Hence the absence of Wallerian degeneration The abundance of neuroglia in the foci justifies the name sclerosis which has been given to the process

These foci are visible on naked eye examination the fresh ones as greyish translucent patches the older ones as greyish or pinkish shrunken areas Grey and white matter are both affected the foci having some predilection for the walls of the ventricles The foci bear no necessary relation to blood vessels

Under the microscope the older patches are found to contain proliferated neuroglia and nerve-fibres which have lost their myelin sheaths. The axis cylinders in the sclerosed areas escape destruction for a long time For this reason secondary degenerations do not occur in the spinal tracts and sections of the cord between lesions at different levels present normal appearances Ganglion cells are also spared, hence wasting of the muscles supplied by the affected segments is not a feature of the disease In recent patches œdema is present with infiltration by lymphocytes plasma cells and compound granular corpuscles around the blood vessels especially in the adventitial sheath of the veins It is highly probable that these inflammatory changes represent the initial lesion and that the alterations in the nerves and in the neuroglia are secondary to them

Symptoms—In the early stages the axis cylinders in the diseased areas are not interrupted completely but suffer partial and temporary impairment which alters in intensity with the severity of vascular and other inflammatory changes in the tissues around them Moreover as the inflammation subsides in one patch a new one develops and produces a different set of symptoms Hence it is not surprising that the earliest symptoms are often slight and fleeting or that they may first appear now in one part and now in another In spite of this however certain symptoms and physical signs appear with remarkable regularity and render disseminated sclerosis in the more advanced stages at least one of the most distinctive and most easily recognised diseases of the nervous system

It is remarkable that though the demyelinating lesions which are often of considerable size occur anywhere in the central nervous system and commonly involve the fillet the lateral fillet, the spinothalamic paths and the peripheral neurones in their intermedullary course and the visual path yet anything but the most transient loss of function seldom occurs in connection with these systems On the other hand the phylogenetically newer systems—the pyramidal paths and the proprioceptive system commonly suffer permanent damage The optic nerve is a common site for the development of an area of the disease This may be situated anywhere between the globe and the optic chiasma and produce the very characteristic picture of acute unilateral retrobulbar neuritis

Motor Symptoms.—Weakness in the lower limbs is the symptom for which many patients first seek relief. Beginning with a feeling of heaviness or stiffness in one or both limbs the weakness, which may be limited at first to one group of muscles increases in some uniformly in a large number with remissions or with periods of apparent recovery until at last after a time which varies from a few weeks to many years, it ends in severe spastic paraplegia. The physical signs are those of pyramidal lesions in general—increased tone in the muscles and exaggeration of the tendon reflexes diminution or loss of the abdominal and cremasteric reflexes and Babinski s plantar response They are of extreme importance for some or all of them may be present when the patient s complaints are still trivial and they are found so constantly in all stages of the disease that the diagnosis of disseminated sclerosis is rarely made in their absence

The paralysis can often be distinguished from that of other pyramidal affections

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Double vision in a young person should always arouse the suspicion of disseminated sclerosis, and if it is associated with signs of pyramidal tract disease, the combination makes the diagnosis almost certain

Strabismus is uncommon Even when the patient is seen whilst complaining of double vision it is unusual to detect any limitation in the range of the ocular movements *Ptosis* is rare

Nystagmus is present in more than half the cases but not so frequently as an early sign It is usually fine rapid and horizontal appearing only when the eyes are directed to the side In some cases the eyes oscillate constantly whatever their position Except in rare cases there is no apparent movement of objects even when the oscillations are of wide range

Visual failure —Diminution of visual acuity due to lesions in the optic nerves—retrobulbar neuritis—occurs sooner or later in many cases It may precede all other symptoms by a period of several years As in the case of the other symptoms it is subject to exacerbations and periods of improvement A young healthy person complains of rapidly increasing mistiness of vision, usually in one eye sometimes in both or in one after the other reaching its maximum in a few hours or days this is often preceded or accompanied by pain about the orbit, which is increased on moving the eye In the common unilateral case the signs are those of a lesion in one optic nerve, the pupil on the affected side is larger than its fellow its direct reaction to light is impaired but it contracts well consensually Tests with a small object preferably coloured reveal a central scotoma At the onset the disk is usually normal but in a few instances the inflammation reaches the nerve head in which event the disk is blurred and swollen Later the disk may be pale or normal Rapid improvement of vision is the rule Special tests may reveal a persistent slight loss of visual acuity and a partial central scotoma or very rarely a complete central scotoma Subsequent acute attacks are common In some cases the onset of visual failure is gradual Usually the defect is slight but it may be serious although complete blindness never occurs In these cases the disk is pale especially in its temporal portion, and the field shows a central scotoma or narrowing at the periphery

Mental Symptoms —Defective memory and slight impairment of intellectual power are common Some of the patients are morose and subject to fits of depression, but the majority are surprisingly cheerful and do not seem to suffer mentally even when their physical state is most pitiable This unjustified cheerfulness is called euphoria In many cases there is considerable loss of emotional control and ready laughter or weeping is fairly common More often there is merely a tendency to laugh at trivial things

Sphincter Disturbances —These troubles arise from interference with the long paths in the spinal cord by which volitional consent and inhibition are held upon the act of micturition Therefore lack of control in the form of hesitancy and precipitancy are common and retention may occur In rare cases control over the rectal sphincter is lost

Other Symptoms —Deafness giddiness and tinnitus sometimes with repeated vomiting are common Epileptiform convulsions are rare In most instances the distribution of the signs will indicate that the lesions are multiple but sometimes although the patches are numerous the signs are those of a single lesion say of the internal capsule of the mid brain or of the cerebellum

Cerebrospinal Fluid —In many cases even when the disease is in an active phase the fluid is normal In others there may be a moderate increase in protein not usually more than 80 mg per cent and a lymphocytic pleocytosis of 10 to 30 per c mm The Lange colloidal gold test is negative in about half the cases In the other half the test is positive and may be of the luetic or paretic type The latter variety may be strongly marked and when occurring in association with a negative Wassermann reaction is very suggestive of disseminated sclerosis

by the variations in its severity from time to time and by the occurrence of remissions or of apparent recovery the improvement sometimes lasting for weeks or months and in rare cases for many years In most cases moreover examination will reveal some other sign—nystagmus intention tremor, or pallor of the disk—which betrays the cause of the paralysis. In one large group of cases particularly common when the disease begins *after the age of 35, the symptoms are those of a steadily increasing* spastic paraplegia without remissions and without any indication, either in the physical signs or in the history of extra pyramidal disease The gait may be but slightly altered even when the tendon reflexes are greatly exaggerated and the plantar responses are extensor Later, it becomes spastic or spastic and ataxic Sometimes ataxy makes walking very difficult, when the power in the limbs is only slightly impaired In the arms there is often loss of power associated with exaggeration of the tendon reflexes *In some cases the arms are affected before the lower limbs* when astereognosis and loss of sense of position from a lesion in the course of the corresponding posterior column of the cord produce one of the commonest of the early symptoms—the useless arm

Tremor —The characteristic tremor in the arms appears on voluntary movement only and increases in rate and amplitude as the goal is approached For these reasons it is called intention volitional or terminal tremor It is sought for by causing the *patient to touch his nose with the tip of one finger In its minimal form the tremor* appears as two or three jerky movements of the finger just as the goal is attained or the finger reaches the nose without any abnormal movement and then oscillates so that it slips away from the nose again or depresses it several times before coming to rest The tremor may be noticed first in writing or in performing other delicate movements such as threading a needle Later the rate and amplitude of the movements increase, and the tremor, although still greatest at the end appears almost as soon as a voluntary *movement begins In advanced cases it prevents all useful* movements and the patient is unable to do anything for himself The arms are affected earliest and most often but nodding of the head is common and any part of the body may be affected Beside intention tremor other types of inco ordination of the limbs are occasionally seen such as those characteristic of lesions of the optic thalamus or of the mid brain or of the cerebellum

Sensory Symptoms —*Subjective* —Numbness and tingling in the extremities and alterations in the sensation of various parts are common complaints. They are often transient and may be the only symptoms during the premonitory period Severe pains are rare, but many patients complain of stiffness or of aching in the limbs and in the back Occasionally intense neuralgic pain of trigeminal nerve distribution is found

Objective —Severe cutaneous sensory loss is not common, but careful examination will often reveal areas of skin in which sensation is impaired Occasionally the loss is severe and may show so sharp an upper level as to suggest the presence of a spinal tumour In many cases the sense of position and passive movements in the limbs is seriously affected in others loss of vibration sense is the only sensory sign An isolated loss of the last named in the legs is a phenomenon of diagnostic importance. Like *the other signs the sensory disturbances often show* considerable variations in extent and degree at different examinations

Ocular Symptoms —Attacks of *double vision* are frequent and highly characteristic of the disease. Close interrogation avoiding the leading question if possible will often elicit an account of these attacks *when the patient has not* mentioned them at first either because he has forgotten them or because it does not occur to him that a symptom so remote or so transient can have any bearing on his present trouble This diplopia is of the highest importance because it is often the sole complaint when the patient seeks advice for the first time and because its presence *or a history* thereof is often the deciding factor in the diagnosis of early cases with spinal symptoms

5 *Spinal syphilis* may also produce a paraplegia of variable onset which may be associated with evidence of scattered lesions elsewhere in the nervous system An examination of the blood and spinal fluid will usually clear up any doubt

6 *Cervical spondylosis* in middle aged and elderly subjects may give rise to a fluctuating lesion of the cervical cord which is very apt to be misdiagnosed as disseminated sclerosis

Course and Prognosis—Despite the remarkable fluctuations which may mark its course the disease ultimately disables the sufferer and is the cause of his death Nevertheless it is important to remember that after the initial outbreak of symptoms some patients regain normal physical capacity lose all abnormal physical signs and lead a normal life for several years 5 10 and 15 year periods of this kind are by no means rare and in general it may be said that the period of evolution of the disease is longer than is generally supposed On the other hand a few cases run a rapidly downhill course from the onset The later in life disseminated sclerosis makes its first appearance the more benign its course and sufferers may be found who have reached old age without gross or total disablement Commonly after two or three fresh exacerbations with intervening recoveries of greater or less completeness a slowly increasing permanent disability sets in It is not possible to say that those cases which run the longest and less distressing course owe this to treatment for many untreated cases fare relatively well But there are certain factors which do appear to influence its course unfavourably in most though not in all instances—thus intercurrent illness especially if it be febrile injuries which disable the patient for a short period, all surgical interventions—including the therapeutic interruption of pregnancy which is designed to avert the frequently seen exacerbations that follow the puerperium—and prolonged or recurrent physical exhaustion

Treatment—The behaviour of disseminated sclerosis makes the assessment of any mode of treatment extremely difficult and a failure to appreciate the wideness of its fluctuations and the length and completeness of some of its remissions is responsible for many therapeutic claims that in the hands of those best acquainted with this malady fail to justify themselves So far there is no remedy which exerts any constant or certain influence upon the course of the disease

The most important general considerations in treatment are to provide complete rest in bed during an acute relapse and to arrange for a sheltered life during periods of remission or when the disease has become established

Of drugs arsenic is the remedy which has had the longest vogue and many believe that it is of value though it cannot in any sense be regarded as curative It may be given as Fowler s solution starting with a dose of min 3 t i d and increasing it to min 8 t i d over a period of 3 to 4 weeks If this method is used it is best to stop all arsenic for a week at the end of each complete course Not every patient can tolerate doses larger than min 3 or min 4 three times daily This method is probably as useful as that of intramuscular injection but considerations of expediency may dictate the use of the latter method

A more recently employed drug is quinine hydrochloride in doses of gr 3 to 5 twice daily continued over a long period Here again intolerance may intervene and prevent this Periodic courses of quinine bismuth iodide have also been advocated Other recent forms of medication include liver therapy pyrexial therapy, protein shock therapy and vaccine therapy None of these has justified itself and when it is recalled that a febrile illness commonly aggravates the severity of disseminated sclerosis it is scarcely surprising that pyrexial therapy should sometimes have the same result

The fact that disseminated sclerosis is sometimes—though not always—adversely affected by a confinement has led to the increasing advocacy of terminating pregnancy at the third month to avert this ill effect But this procedure is exposed to the same objection as a full term delivery or any surgical procedure and sometimes has the

Diagnosis —The combination of spastic weakness of the legs with Charcot s triad of symptoms—namely intention tremor nystagmus and scanning speech—which is so widely and so erroneously regarded as characteristic of the disease and as necessary to its recognition is rarely seen except in the later stages of disseminated sclerosis As this malady usually presents itself to us in its initial stages when it may and should be diagnosed it commonly consists in a group of signs of involvement of the pyramidal tracts namely increased tendon jerks Babinski plantar responses absent abdominal reflexes a little weakness of dorsiflexion of one or both feet possibly also some weakness of flexion of the proximal segments of the lower limbs and usually a degree of impairment or loss of vibration sense over the malleoli. In many cases this is all we can find, but in an otherwise healthy young adult it is a syndrome more likely to be due to disseminated sclerosis than to any other pathological process

Perhaps there may be confirmatory signs such as a little nystagmus, slight intention tremor or sensory ataxy of an arm it may be pallor of the temporal half of one or of both disks—a pathognomonic sign. If some or all of these signs have as it were been arrived at after such a fluctuating course as we have seen to be so typical of most cases of disseminated sclerosis, then diagnosis can be no longer in doubt and it is comparatively seldom that pathological examinations of blood or cerebro spinal fluid are really necessary for this end

When after some years, the disease is fully developed it still retains its individuality The patient is commonly euphoric there is frequently tremor of the head, and sometimes of the whole body when the patient tries to stand or walk The arms are unsteady the legs spastic and weak—sometimes showing a tendency to pass into the condition of paraplegia in flexion There is little sphincter control left but cutaneous sensibility is commonly almost or quite intact

At whatever stage disseminated sclerosis comes under observation a careful enquiry into the history of the illness is important and to elicit this requires a knowledge of the natural history of this disease as it has been outlined here

Disseminated sclerosis has to be diagnosed from various diseases of which we will consider the following

Hysteria —The serious mistake of attributing the early symptoms of this relentless disease to hysteria can be avoided by the taking of an accurate history combined with a careful examination of the nervous system Pallor of the disk absence of the abdominal reflexes or a distinct difference between them at corresponding points on opposite sides unequal exaggeration of one or more of the tendon reflexes when compared with their fellows an extensor plantar response on one or both sides—any one of these signs alone would render a diagnosis of hysteria untenable

Compression of the cord.—When the signs in disseminated sclerosis are purely spinal the diagnosis from *spinal tumour* presents real difficulties The first may be mistaken for the latter when the paralysis increases steadily without remissions and is associated with sensory loss extending upwards to a definite level while the reverse error may be made when the symptoms caused by a tumour are purely motor or vary in intensity or are associated with nystagmus

Friedreich s ataxia.—This may be suggested by the presence of ataxy in a young patient with disseminate sclerosis The distinction can be made at once for in the latter disease the tendon reflexes in the lower limbs are exaggerated whereas they are lost early in Friedreich s disease

Subacute combined degeneration of the cord —In the rare cases where disseminated sclerosis has its onset in middle aged subjects the combination of manifestations indicative of involvement of the posterior and lateral columns of the cord together with the presence of paraesthesia may closely simulate subacute combined degeneration. Investigation of the blood for changes of pernicious anæmia and of the gastric juice for free HCl will usually render the differential diagnosis certain

may become stationary and in rare instances proceed to complete recovery of both power and of vision or the subject may be left with disability of varying severity

The paraplegia is that characteristic of a diffuse spinal lesion in that there is sensory loss, paralysis and loss of sphincter control

Treatment—No treatment has any clear influence upon the course of events Arsenical preparations have been employed—as for disseminated sclerosis The management of the case is that of any case of paraplegia

HEREDITARY AND FAMILIAL DISEASES

1 FRIEDREICH S ATAXIA

Synonyms—Friedreich s Disease, Hereditary Ataxia

Definition—An hereditary disease characterised clinically by a progressive ataxia and pathologically by the degeneration in the spinal cord of the posterior columns lateral columns (pyramidal tracts) and spino cerebellar tracts and in the cerebellum of a number of the Purkinje cells

Ætiology—Transmission occurs both through the males and the females In direct heredity is the most common for the reason that the subjects of this disease are usually afflicted in childhood and incapacitated by the time adult life is reached and therefore they do not procreate Direct heredity is however by no means so uncommon as has been supposed Isolated cases in which no heredity can be traced are not rare The first signs of the disease usually appear in early childhood and before the sixth year but symptoms may not be evident until a few years later In a considerable number of cases however the onset is delayed until the time of puberty while in a few examples it may be delayed until after the age of 30 years As a rule the age incidence is approximately the same in each child rank of the same family but sometimes the phenomenon of ' anticipation is well marked the disease appearing at an earlier age in each succeeding generation The disease is said to be slightly more common in males

Pathology—The spinal cord is unusually small and apparently this smallness may be congenital and the posterior roots tend to be small grey and poorly myelinated The essential change is a primary degeneration of certain neurones in the dorsal column of the spinal cord of the pyramidal tracts and of the spino cerebellar tracts both dorsal and ventral This degeneration commences first in the periphery of the axon which slowly dies back towards the nutrient cell body

The degeneration of the dorsal columns is usually the earliest change and remains the most prominent feature throughout The degeneration of the fibres of the pyramidal tract appears later

The spino cerebellar tracts are constantly degenerated the direct cerebellar tract being the most seriously involved The cells of Clarke s column from which the direct cerebellar tract takes origin and around which the pyramidal tracts end degenerate and disappear as does also the network of collaterals which surrounds these cells Consequent upon these degenerations and secondary to them well marked neuroglial proliferation or sclerosis occurs The cerebellum may be normal or it may show varying degrees of atrophy of Purkinje s cells or of any other of its cell elements and of the tracts connected therewith

Symptoms—The onset is always insidious and physical signs of abnormality usually precede any complaint on the part of the patient or his relatives The first symptoms are generally complained of between the sixth and the tenth year of child hood but if a careful examination be made of the younger members of the families upon which Friedreich s disease is incident, physical signs of the disease especially

same unfortunate influence upon the course of the malady It is therefore not a therapeutic measure that can be justified by its results The correct procedure is to take every possible measure to maintain the health and nutrition of the pregnant woman and to afford her at this time and after the puerperium more than the ordinary amount of rest This is the rational, if not always the acceptable line of treatment Further women suffering *from the disease in an active phase should* be advised against becoming pregnant

Of great importance is the right ordering of the patient s life when practicable, and the avoidance of fatigue in the early stages of the disease

OTHER DEMYELINATING DISEASES OF THE NERVOUS SYSTEM

There exist a number of other diseases of the central nervous system having considerable pathological affinities with disseminated sclerosis in that they depend upon a demyelinating process predominantly of the white matter which may be either diffuse or localised and predominantly cerebral or spinal in incidence

Of these disorders Schilder s disease in which the morbid process is confined to the brain (p 1412) and acute encephalomyelitis associated with acute specific fevers (p 1411) the incidence of which may fall on either the brain or spinal cord or upon the two together *have already been considered in the article on encephalitis*

There remains for consideration the syndrome of neuromyelitis optica.

There are points of considerable resemblance between these three disorders and disseminated sclerosis particularly as regards their pathology but there are equally significant points of difference and whether or not they are ætiologically related cannot at present be affirmed

NEUROMYELITIS OPTICA

Synonyms —Diffuse Myelitis with Optic Neuritis Devic s Disease

Definition —A form of dis eminated myelitis preceded or accompanied by retrobulbar neuritis with or without papillœdema It is commonly acute in onset and may end in death or in arrest with residual disabilities Complete recovery is rare Persons of all ages from adolescence onwards may be affected

Ætiology —Nothing whatever is known of its causation and therefore it has been suggested that the disease is infective None of the neurotropic viruses is *known to produce the demyelination which is* the characteristic lesion of the disease nor is there any evidence that this is bacterial

Pathology —The spinal cord shows either diffuse or multiple disseminated lesions They may be confined to a few segments of the cord or may be found from end to end of this structure The essential feature of the lesions is a demyelinisation of axis cylinders There is also round celled perivascular infiltration an intense proliferation of microglial cells and a multiplication of tiny vessels in the affected areas The optic nerves *present the same type of lesion* namely an intense demyelinisation of the nerve fibres In general the pathological changes are more intense than those of disseminated sclerosis and show less evidence of partial remission

Symptoms —The blindness which indicates the optic nerve lesion may precede or may follow the appearance of paraplegic symptoms *The latter develop rapidly* and may spread upwards until sensory loss and muscular weakness reach the upper thoracic level Blindness with some swelling of the optic disk and central scotoma may ensue The patient may become progressively worse and die or the paralysis

first objective sign of the disease but in cases in which there is a major degeneration of the pyramidal tracts the knee jerks may persist or even be brisk into the advanced stages of the disease The abdominal reflexes gradually disappear The plantar reflex is invariably an extensor response The sphincters usually escape The cerebrospinal fluid presents no abnormality

Spinal curvature is very common and may reach a severe degree It consists of a scoliosis of the dorsal region and often with some kyphosis and with a compen satory reverse lumbar curve The cause of this deformity is probably the defect in the postural tone of the muscles

Diagnosis —In uncomplicated cases the diagnosis is a matter of no great diffi culty on account of the strikingly distinct nature of the symptoms Friedreich s disease can hardly be mistaken for tabes since the history of heredity the peculiar deformity of the feet and spine the extensor plantar reflex the speech affection and the nature of the ataxy contrast strongly with the loss of pain sensibility and of deep sensibility the pupillary changes the sphincter trouble the abnormal Wassermann reactions and the abnormal cytology of the cerebrospinal fluid in tabes The dis tinction from disseminated sclerosis presents more difficulty but in this disease the onset never occurs in childhood there is no heredity the deep reflexes are never lost and the spinal deformity does not occur

Course and Prognosis —The course of the disease is usually progressive in slow and irregular fashion and the prognosis is therefore in every case serious but the average duration of the disease is over 30 years and in some cases it seems to have no tendency to shorten life The prognosis is worse and the course more rapid in those patients who have shown disability from the time of learning to walk In some cases the disease appears to become arrested Intercurrent maladies febrile illnesses and debilitating influences generally may have an effect in hastening the advance of the disease and bringing about a fatal termination Confinement to bed from any cause whatever has a bad influence upon the ataxy and upon the capacity for walking

Treatment —No treatment is known which specifically affects the malady General tonic treatment and all measures which improve the general health and mental well being often have a surprising effect in improving the ataxy Re educa-tional training of the limbs and trunk in the form of Frenkel s exercises are most beneficial Properly designed boots to ensure the most advantageous use of the deformed feet must be provided

2 DELAYED CFREBELLAR ATROPHY

Of all the primary atrophies of the cerebellum it may be said that their ætiology is unknown but the cause probably endogenous In some forms there is clear evidence of heredo familial factors but not in all Some of them appear in early infancy while others manifest themselves in later life and are hence called delayed The infantile forms are extremely rare Of the delayed varieties much the least uncommon is an atrophy of the cerebellar cortex—*Marie s delayed cortical cerebellar atrophy*

Ætiology and Pathology —This disease affects both sexes and shows itself at any age from 45 onwards The lesion is bilaterally symmetrical and is most marked on the upper anterior parts of the cerebellum It is essentially a cortical atrophy with disappearance of the Purkinje cells as its characteristic feature Familial incidence has been described by Holmes and others

Symptoms —The clinical picture is that of a slowly developing ataxia of gait accompanied by a disorder of articulation ataxia of the upper limbs develops later but nystagmus rarely occurs In many cases the tendon jerks are exaggerated indi cating an element of spinal degeneration

the extensor response in the plantar reflex the retraction of the great toe and some degree of pes cavus may often be found before the sixth year

Ataxia is always the first sign to appear and this is shown by an awkwardness of gait and a tendency to stumble and fall readily Sometimes it is obvious from the history that the ataxy dates from the earliest years of infancy when it is said that the child was never strong on his legs from the time of learning to walk and that he could never run properly or join on equal terms with other children at play As the disease progresses the gait slowly becomes more irregular and clumsy The patient walks with his feet upon a broad base and staggers and reels from side to side but notwithstanding this he keeps a fairly direct line of progression He takes short steps which are unequal and which are irregular in relation to the line of progression and the movement of each foot as it is raised is poorly co ordinated There is never the undue excursion and noisy stamping of the feet which are so characteristic of the gait of tabetic patients

In standing the body oscillates from side to side in slow and clumsy fashion and coarse tremors of the head and trunk are constant features in advanced cases (titubation) Sometimes Romberg s sign is present but this is never so well marked as in tabes and it is frequently absent The ataxy invades the upper extremities as a rule, later than the legs There is first clumsiness with the finer movements and then little by little with all the movements It closely resembles the ataxia due to gross disease of the cerebellum and differs from that which occurs in tabes That irregular breaking of a movement towards the end of its accomplishment which has been long termed intention tremor ', is frequently seen

Irregular involuntary movements, often described as like those of chorea or of myoclonus occur in advanced cases and are most frequently seen in the head and neck as nodding movements and jerky tremors Nystagmus is usual it is generally seen with lateral deviation of the eyes and may be very irregular Dysarthria is almost constant and is gradually progressive At first the speech is of the slurred cerebellar type but with increasing ataxia it becomes scanning or drawling

The strength of movements is at first little impaired but as the disease advances and the pyramidal degeneration increases the power is gradually lost in proportion to the degree of the pyramidal degeneration which varies greatly in different cases The lower extremities are affected first and most and later the arms and in severe cases at a late stage paralysis may be almost universal

The condition of the muscular tone depends upon the relative degree of degenera tion in the posterior roots and in the pyramidal tracts respectively the former tending to abolish and the latter to increase it As a rule the influence of the posterior root degeneration is preponderant and therefore the limbs are flaccid and hypotonic but occasionally they are somewhat rigid Contractures are the rule but these are confined to the lower extremities The most constant of these produces the char acteristic pes cavus Moderate wasting of the small muscles of the feet and hands is not very uncommon Sensibility is but little affected but in most cases minute examination reveals slight relative loss to touch pain and temperature most marked at the periphery of the limbs and diminishing upwards Similarly there may be slight loss of sense of position in the limbs and diminished vibration sense

The ocular movements are almost always intact apart from the already described nystagmus In rare instances strabismus diplopia and ptosis have been recorded The pupils are not affected Optic atrophy is a rare phenomenon in Friedreich s disease yet it has been reported in quite a number of otherwise typical cases

Mental symptoms are usually not conspicuous but some of the patients are of poor mentality from the first while others show a tendency to severe mental degenera tion in the later stages of the disease Emotional instability irritability and outbursts of temper may occur

Absence of the tendon reflexes is a most characteristic feature and is often the

spot in the region of the macula and in addition optic atrophy occurs later and (4) a fatal termination in the marasmic state before the age of 2 years

Ætiology —Nothing is known of the ætiology of the disease apart from its familial and racial incidence The tendency to the disease is unquestionably congenitally installed

Pathology —This is very striking It consists of a progressive degeneration of the nerve cells from the highest to the lowest and ultimately there may be no normal cells remaining anywhere in the nervous system The degeneration takes the form of swelling of the cell protoplasm and of the dendrites with chromatolysis swelling of the hyaloplasm and destruction of the cell fibrils followed by disappearance of the nucleus and finally by absorption of the remains of the cell The degenerating nerve cells are characterised by the accumulation of granules of lipoid substances which resemble those observed in other cells of the body in Gaucher s disease Niemann-Pick s disease and the Hand Schuller Christian disease Every cell of the central nervous system both of the brain spinal cord and spinal ganglia is in the end similarly affected

Symptoms —There are few diseases in which the *clinical manifestations* are so perfectly uniform as in this malady The children have all been born at full term and in perfect health They thrive well during the first 3 to 6 months of life when *they gradually become listless and apathetic cease to take interest in the surroundings* and begin to show signs of the visual failure which ends in blindness Later the child is unable to sit up or to hold up its head The limbs which may be slightly spastic at first become flaccid and motionless There is a gradual increase of all these signs The mental defect becomes more and more noticeable the paralysis more extreme complete blindness follows and the patient sinks into a condition of marasmus in which he dies Convulsions nystagmus and strabismus are sometimes present

The retinal changes are pathognomonic and are due to a degeneration and dis appearance of the nerve cells of the retina and their processes which constitute the fibres of the optic nerve This change is most intense in the region of the fovea centralis where the retina thins and disappears over a circular area exposing the vascular choroid This gives rise to the characteristic appearance on ophthalmoscopic examination of a cherry red spot in the region of the macula This spot is actually a hole in the retina exposing the choroid The optic disk shows progressive atrophy

Diagnosis —Distinction has to be made between this and other forms of pro gressive diplegia The symptoms are so distinct that a physician who is acquainted with the disease and able to recognise the retinal picture can hardly fail to make the correct diagnosis

Treatment —No treatment is of any avail

2 OTHER FORMS OF CEREBRO MACULAR DEGENERATION

In addition to the classical infantile form described in the preceding article two other forms are well known in which the pathological changes are similar but much less severe than in the Warren Tay Sachs disease and there is also a similar familial incidence but the onset of the malady occurs later in life and the course is less rapid and the result far less serious The later the onset in life the slighter and less progressive are the symptoms The cherry red spot at the macula so constant in the infantile form does not occur in the later forms The characteristic retinal change is a disturbance of the retinal pigment commencing in the macular region rather like retinitis pigmentosa accompanied by honeycomb changes at the macula and sometimes by optic atrophy The *juvenile* form occurs in later childhood and is characterised by the association of the retinal changes and visual defect with some degree of mental deterioration The *adult* form is the least progressive of any and the clinical

Diagnosis —With the foregoing features it is natural that the disease should frequently be mistaken clinically for disseminated sclerosis The later age incidence the absence of nystagmus of disk changes of spasticity and of loss of sense of position and the steady progress of the malady should make the diagnosis of disseminated sclerosis untenable while the reeling character of the ataxia and the sibilant instead of staccato quality in the articulation disclose the real nature of the disease In tabes dorsalis, with which it may be confused because of the ataxia numerous characteristic signs are present by the time ataxia becomes pronounced, and dysarthria is not a feature of tabes

Treatment —No treatment is known to have any effect on the degenerative process

3 FAMILIAL SPASTIC PARALYSIS

Ætiology —This rare disease is sometimes hereditary but is more commonly familial and incident upon several children of the same parents Sporadic cases also occur The onset is gradual in early life, and usually occurs after the sixth year

Pathology —The pathological changes consist in a primary degeneration of the pyramidal neurones which apparently takes place in terms of the length those supplying the lumbo sacral region being lower and longer are earliest affected those supplying the brain stem being shortest are the last to be affected Degenerative changes in the neurones of the posterior columns of the spinal cord are often present *showing the transition to the pathological type of the hereditary ataxies*

Symptoms —The clinical aspect consists in the slow development of spasticity and weakness first and most in the legs which gradually increases and progresses to the trunk and upper extremities and involves the face last and least The usual signs of pyramidal involvement are present in the loss of abdominal reflexes increased deep reflexes and extensor type of plantar reflex The malady is progressive increasing to complete paralysis and in its course contractures of the spastic muscles occur that of the foot and leg producing some degree of pes cavus while, above this flexor contracture at hip and knee is met with Optic atrophy is by no means uncommon Mental symptoms do not occur in uncomplicated cases neither is epilepsy observed

Diagnosis —This malady is most easily confused with cerebral diplegia but the latter disease appears much earlier as soon after birth in fact as defective movement in the child can be ascertained Further cerebral diplegia is not a progressive disease in the majority of the cases and *it is often associated with mental deficiency* and recurring convulsions

Treatment —This is the same as that of Friedreich s ataxia except that the purpose of exercises if given should be to secure the best use of the spastic lower limbs *instead of to overcome ataxia*

4 CEREBRO MACULAR DEGENERATION

1 THE INFANTILE FORM

Synonyms —Warren Tay Sachs Disease Amaurotic Family Idiocy

Definition —A family disease of infancy occurring chiefly but not entirely in the Hebrew race *affecting children during the first year of life* who are apparently quite healthy when born and characterised by—(1) progressive mental impairment ending in absolute idiocy (2) progressive paralysis of the whole body (3) progressive diminution in sight, ending in absolute blindness *Pathognomonic retinal* changes are constantly present consisting of a large and conspicuous cherry red

spot in the region of the macula and in addition optic atrophy occurs later and (4) a fatal termination in the marasmic state before the age of 2 years

Ætiology—Nothing is known of the ætiology of the disease apart from its familial and racial incidence The tendency to the disease is unquestionably congenitally installed

Pathology—This is very striking It consists of a progressive degeneration of the nerve cells from the highest to the lowest and ultimately there may be no normal cells remaining anywhere in the nervous system The degeneration takes the form of swelling of the cell protoplasm and of the dendrites with chromatolysis swelling of the hyaloplasm and destruction of the cell fibrils followed by disappearance of the nucleus and finally by absorption of the remains of the cell The degenerating nerve cells are characterised by the accumulation of granules of lipoid substances which resemble those observed in other cells of the body in Gaucher s disease Niemann-Pick s disease and the Hand Schuller Christian disease Every cell of the central nervous system both of the brain spinal cord and spinal ganglia is in the end similarly affected

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Treatment.—No treatment is of any avail

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manifestations are the visual defect and retinal changes in the absence of mental deterioration

5 HEPATO LENTICULAR DEGENERATION

Synonyms —Progressive Lenticular Degeneration Wilson s Disease

Definition —A rare progressive disease of the nervous system often familial characterised by involuntary movements rigidity and hypertonicity, with contractures without signs of pyramidal disease and by dysarthria dysphagia emotionalism and progressive *emaciation* Several closely related clinical forms of the disease bear distinctive names *tetanoid chorea* (Gowers) *pseudosclerosis* (Westphal) *progressive lenticular degeneration* (Wilson) and *torsion spasm* and *dystonia musculorum deformans* (Thomalla) Cirrhosis of the liver occurs in all forms The Kayser Fleischer zone of corneal pigmentation occurs in the first three forms but has not yet been recorded *in torsion spasm* The most constant nervous lesions are found in the corpus striatum

Ætiology —The disease often occurs in children of the same parents but there is no evidence that it is congenital or hereditary The age of onset has been as early as 7 years and as late as 26 years The primary and essential lesion is in the liver, its cause is unknown Syphilis is not a factor

Pathology —A *multilobular* cirrhosis with 'hobnail' liver is always found after death There is good evidence that the cirrhosis is not slowly progressive but is the result of a number of attacks of acute hepatitis The hepatitis has caused death in some members of affected families before nervous symptoms appeared The nervous lesions are purely degenerative In Wilson s cases they were almost confined *to the lenticular nucleus especially the putamen Every degree of degeneration* was seen from discoloration and sponginess of the nucleus in rapidly fatal cases to shrinkage and atrophy and even to complete disintegration and excavation of the ganglion Later observers have described lesions in many other parts of the nervous system The lesions are often most intense in the corpus striatum but the noxious agent has *no strictly selective action on any one anatomical group of ganglion cells or on any* limited area of the nervous system It is now known that the degenerate basal ganglia contain excessive amounts of copper compounds and that there is a persistent excess of this element in the urine as well as an increased urinary excretion of amino acids

Symptoms —In many cases there are no symptoms of disorder of the liver during *life In other cases an account is obtained of symptoms referable to acute hepatitis* before the onset of nervous symptoms—attacks of diarrhœa and vomiting pyrexia jaundice migrainous headaches hæmatemesis and sometimes definite ascites

The first nervous sign to appear is usually involuntary movement of the extremities which may be of several kinds In progressive lenticular degeneration rhythmical tremors increasing on voluntary movement furnish the most common symptom This is followed by rigidity of the face the muscles of the neck and later of the trunk which rigidity *increases steadily until the patient becomes helpless* The rigidity of the face and neck muscles gives rise to a peculiar expressionless appearance *Still* later extensive contractures usually in the flexed position in the upper and lower extremities follow but sometimes there is extensor contracture of the latter During sleep the tremors cease but the contractures do not relax Dysarthria of a slurring type, *results from affection of the muscles of speech* and may end in complete anarthria Progressive muscular weakness and general emaciation follow and the patient becomes emotional *facile docile and childish There is no* fibrillation or localised amyotrophy The optic disks and pupillary reactions are normal There is an absence of nystagmus cerebellar symptoms and impairment of *sensation* The reflexes are not altered as in the case in pyramidal disease

Prognosis —The disease always ends fatally in a few months or years the *average duration is about 4 years*

Treatment—No curative treatment is known but there is evidence that symptoms are improved and the progress of the disorder delayed by treatment with dimercaprol (British Anti Lewisite)

6 KERNICTERUS

Definition and Ætiology—A yellow pigmentation of certain of the basal ganglia associated clinically with motor disorders of the type known as extra pyramidal and found as a rare phenomenon in children who normal at birth develop jaundice within the first 3 days of life

In neonatal jaundice the brain may be diffusely pigmented or more rarely the pigmentation may be confined to the putamen subthalamic and dentate nuclei the cornu Ammonis and fascia dentata To the latter variety of jaundice of the brain the name kernicterus has been given by Schmorl The nerve cells in the affected masses of grey matter show evidence of destruction and degeneration while the nerve fibres are demyelinated

Symptoms—The child is healthy at birth but within a few days develops intense jaundice usually the form known as hæmolytic disease of the new born (see p 745) and now known to be due to Rhesus incompatibility between the parents though kernicterus has been found in association with septic jaundice The onset of jaundice is followed within 24 hours by tonic and clonic movements muscular rigidity and opisthotonos alternating with periods of flaccidity If the child survives involuntary movements of choreoathetoid form develop within a few weeks Emotional instability and mental retardation appear as the child grows older

Diagnosis—Athetosis and comparable forms of involuntary movement are not rarely seen in children and are in the majority of instances not associated with kernicterus Yet when a case of such motor disorder is seen in a child in respect of whom there is a history of neonatal jaundice the possibility of this disease should be borne in mind Again the development of marked symptoms of organic nervous disease immediately after the appearance of severe jaundice in a newly born infant should lead to a consideration of this condition as the probable pathological basis

Prognosis—There is a marked tendency for these patients to die during infancy or childhood of intercurrent disease but a minority survive to adult life with a varying degree of mental impairment and disorder of movement

Treatment—There is no curative treatment and endeavour should be directed towards education and towards training in co ordinated movements In cases where sufficient intelligence exists much can be done by patient training especially in the hands of trained workers

7 NEUROFIBROMATOSIS

Synonym—Von Recklinghausen s Disease

Definition—A complex disorder involving principally the skin and nervous system and characterised in the former by the development of abnormal pigmentation and a great variety of tumours and in the latter by the presence of multiple neurofibromata in the peripheral and less frequently the central nervous system

Ætiology—The disease is both hereditary and familial though isolated cases occur Formes frustes are common Although the characteristic features evolve during the life of the patient the malady undoubtedly results from congenital abnormality It is often associated with other congenital and developmental anomalies of the nervous system and skeleton and subjects of the disease show a remarkable propensity for neoplastic disorders

Pathology —The cutaneous lesions comprise fibromata many of which are degenerate nævi and areas of pigmentation In the nervous system multiple fibromata occur in the peripheral and cranial nerves and in addition meningeal tumours and gliomata of the brain and spinal cord may be found

Symptoms —Of the essential features of the disease the cutaneous lesions are usually the first to make their appearance Some may be present at birth others develop during childhood, adolescence or adult life They present a great variety of forms Abnormal areas of pigmentation are commonest These have the appearance of *cafe-au lait* patches and vary in size from a mere freckle to a large zone involving a whole limb Many are between the sizes of a sixpence and a shilling The cutaneous *tumours appear* gradually Some are pedunculated or sessile fibromata often pigmented and usually soft to the touch Others are nævoid in composition They may attain great size coming to form the large redundant folds of tissue known as *plexiform neuromata* The fully developed cutaneous picture is that known as molluscum fibrosum

The tumours on the nerve trunks are also fibromata but usually firmer than these in the skin They may occur on any of the peripheral nerves the limb plexuses or the intra pinal portions of the nerve roots Those peripherally situated are usually painless and seldom interfere with the function of the nerve on which they grow They are occasionally painful on pressure Those which originate on the spinal nerve roots produce the picture of spinal compression commonly preceded by a long period of root pain They are frequently multiple Within the cranial cavity neurofibromata are most often met with on the acoustic nerves but may occur on any of the cranial nerves and produce symptoms characteristic of their position

Von Recklinghausen s disease is often found in association with other congenital anomalies such as spina bifida meningocele cervical rib syringomyelia mental deficiency and epilepsy

The tumours are liable to undergo malignant degeneration and it is not uncommon to find other tumours, such as meningiomata and gliomata in patients with this disorder

Course and Prognosis —In many cases the condition is compatible with a long and relatively normal life though there is a tendency towards slow progression Danger to life results only from central lesions in the cranial or spinal cavities or from the rare malignant degeneration in the peripheral tumours

Treatment —Nothing is known to modify the natural course of the disease Central tumours should be removed surgically as they arise and cosmetic improvement can often be achieved for the cutaneous and subcutaneous lesions

8 TUBEROSE SCLEROSIS

Synonyms —Adenoma Sebaceum Epiloi

Definition —A condition characterised clinically by the symptom triad of multiple cutaneous tumours of the cheeks and face mental deficiency and epilepsy and pathologically by the presence in the brain of areas of gliosis of a peculiar type

Ætiology —Hereditary and familial incidence is common but many i olated cases occur No other factors are known The sexes are equally affected

Pathology —The characteristic lesions of the brain consist of nodular tuberous masses which are most plentiful under the ependyma of the ventricles into the cavities of which they project like candle gutterings Similar nodules can be seen and felt scattered throughout the cortex and rarely in the cerebellum or spinal cord They consist of dense tangles of neuroglia cells many of markedly pathological type The cutaneous tumours consist of an overgrowth of the sebaceous glands embedded

in nævoid and fibrous tissue Tumours also occur in other tissues namely rhabdo myomas in the heart and kidneys and the so called phakoma in the retina

Symptoms —These usually make their appearance in early childhood Varying degrees of mental defect from feeble mindedness to idiocy are universal Epilepsy usually begins within the first few years of life and though any form may occur generalised convulsion is the commonest The characteristic skin lesions make their appearance during childhood in the form of numerous verrucose shotty papules on the butterfly area of the cheeks and nose These are red or reddish brown in colour and the intervening skin is red and shiny The extent and degree of this condition of sebaceous adenoma becomes more marked as the child grows older Numerous other cutaneous tumours and congenital anomalies similar to these occurring in Von Recklinghausen s disease are met with

Course and Prognosis —The course is very slowly progressive Most cases spend their lives in institutions for mental defectives but frequently attain a considerable age

Treatment —Symptomatic treatment is indicated for the epilepsy and when possible procreation should be vetoed and the patient cared for in a suitable institution

CEREBRAL DIPLEGIA

Synonyms —Congenital Spastic Paralysis Lobar Atrophic Sclerosis

Definition —A group of clinical conditions dependent upon lack of or imperfect development or degeneration of the nerve cells of the cerebral cortex basal ganglia or cerebellum This agenesia of nerve cells may affect those cells of the pyramidal system which are the latest to develop before birth namely those for the supply of the lower extremities and the resulting clinical condition is cerebral spastic paraplegia or Little s disease or all the cells of the pyramidal system may be affected producing generalised spastic rigidity Again the higher regions of the cortex may be affected and the result is congenital idiocy Similar affections of the cells of the basal ganglia result in congenital bilateral athetosis and congenital chorea When the cerebellum is involved congenital cerebellar ataxy results Further there may be any combination of the above conditions

Ætiology —The malady may be apparent at the time of birth as the child may be born with contractures present More often the signs of deficient or perverse movement or of mental deficiency appear during the first year of life as the signs of cerebral activity commence to be exteriorised In most cases no heredity can be traced but sometimes several children of the same mother may be affected and direct heredity has been known

Abnormalities of birth are frequent Premature or precipitate birth prolonged birth from uterine inertia rather than from dystocia and asphyxia neonatorum are all common The child is frequently the first born of its mother

Collier has expressed the probable pathogenesis of cerebral diplegia as follows If we regard the brain from the time of its earliest stages of development as a field sown with seeds (neuroblasts) which germinate at different periods of fœtal life and the germination is not even complete at the time of birth the germination of all the elements in due time and their complete development being neces ary for the formation of the perfect brain then we may liken the cause of diplegia to some baneful influence such as a frost which acting at a particular time may spare those seedlings which are well developed and able to withstand it and those seeds as yet not germinated but which causes havoc among the tender germinating seedlings either to their death or severe maiming In some cases as for example in Little s disease the neuroblasts thus affected may after a period of retarded development ultimately become strong plants and complete their development It is of interest that in the

highest degrees of cerebral agenesia—anencephaly, pituitary abnormalities seem to be constant

A well defined variety of cerebral diplegia associated with congenital deafness is now known to occur as a result of the mother suffering from rubella in the early months of pregnancy

Pathology —The essential histology of the affected regions is that of non development paucity in numbers and degeneration of the nerve cells with corresponding absence poor development degeneration or a combination of these states of the tracts which spring therefrom The pyramidal tract, for example, may be found absent throughout, or it may reach to the medulla, or to the cervical region only and so show at what period development was arrested The changes in the nerve cells are followed by secondary gliosis The final result is termed atrophic sclerosis More often certain regions are profoundly affected, while others escape relatively or completely, but the distribution is always symmetrical upon the two hemispheres The convolutions are unduly hard to the touch and their surfaces often present a worm eaten and faceted appearance This irregular form of the convolutions with wide, separating sulci, gives the brain a characteristic appearance, like that of a walnut kernel

Symptoms —The clinical picture of the several forms of cerebral diplegia presents a combination in varying degrees of certain characteristic symptoms always bilaterally distributed though sometimes more severe on one side than on the other These symptoms are muscular rigidity paresis perverse movements contractures and increased deep reflexes Mental deficiency optic atrophy and ataxy are other important symptoms The signs of the disease become obvious during the first year of life or soon after In severe cases soon after birth the nurse in washing the child is the first to notice the stiffness of the limbs or the regular assumption of a curious bodily attitude Otherwise the abnormalities may not be obtrusive until the child should sit up or learn to get about, when weakness rigidity perverse movements and pes cavus may call attention or backwardness in learning to walk and to talk, and mental deficiency may first suggest that there is something wrong with the child The following are the common types of the disease but it must be remembered that any combination of or transition between the types may be met with

1 *Generalised rigidity general congenital spastic paralysis* —There is extensive defect of the pyramidal system The rigidity and weakness affect the whole of the musculature

2 *Paraplegic rigidity congenital spastic paraplegia Little s disease* —The pyramidal deficiency is confined to that supplying the lower part of the trunk and lower limbs

3 *Congenital bilateral athetosis and congenital chorea* —The agenesia affects the cells of the basal ganglia with the appearance of irregularity of movement and of spontaneous involuntary movements which may be of an athetotic choreic or irregular type A certain variable degree of general rigidity is present in these cases

4 *Congenital cerebellar ataxy* —The agenesia affects the cerebellum with the appearance of cerebellar ataxy In this type the limbs are flaccid and in mixed cerebral and cerebellar types there is a tendency to hypotonicity of the muscles instead of rigidity

5 *Congenital idiocy restless idiocy* —The agenesia affects those parts of the brain concerned with the higher functions These children are emotionless restless and unteachable The skull often shows frontal or occipital microcephaly

6 *Microcephalic idiocy*—where the agenesia is of the whole brain and the skull remains very small

Paresis and Rigidity —Except in severe cases in which the weakness amounts to complete paralysis there is more rigidity than weakness and it is often astonishing that there should be so much power in the presence of such a degree of rigidity

The lower extremities are generally the most affected the upper to a less degree and the facial region still less Movement is slow and clumsy and spontaneous involuntary movements are often present in the limbs Contractures accompany the rigidity, and if walking is possible the gait is digitigrade from contraction of the calf muscles, the knees are flexed from contracture of the hamstrings the thighs are rotated inwards and the knees pressed together rubbing against one another More severe adductor spasm gives rise to the cross legged progression The rigidity and contractures when severe may give rise to peculiar attitudes and deformities A mask like expression of face with wide palpebral apertures and large open mouth is not infrequent Slobbering is very common The head may be rigidly retracted but more commonly the chin is pressed down upon the chest The spinal column generally shows some deformity in the way of kyphosis lordosis or scoliosis and pes cavus or equino varus is the rule

PERVERSE MOVEMENTS —Under this heading must be grouped the very constant maladroitness of voluntary movement the facial over action and grimacing in speech and in mimetic expression choreic movements athetotic movements and intention tremor Common sensation and the muscular sense are unimpaired The sphincters are unaffected The deep reflexes are increased but are often difficult to obtain when rigidity is very marked The trunk reflexes are often absent the plantar reflexes usually are extensor in type Since the growth of the skull follows and conforms with that of the brain cranial abnormalities are common There may be microcephaly asymmetry and flattening in the region of the central convolutions or a furrow corre sponding with the interhemispheric fissure or frontal or occipital smallness and flattening Every degree of mental reduction may be met with from slight mental dullness to complete amentia But this by no means corresponds with the severity of the bodily symptoms for the mental defect is often most severe when the bodily symptoms are slight and conversely In some cases very high intelligence persists when there is utter uselessness of the limbs and when speech is hardly intelligible Primary optic atrophy occurs in a small number of cases Inequality of the pupils and slowness of light reaction are not uncommon Nystagmus is often met with Convergent strabismus occurs in about one third of the cases Convulsive attacks are of common occurrence and in about one eighth of the cases epilepsy becomes established

Diagnosis —When the symptoms are well marked the diagnosis presents little difficulty since the disease dates mostly from birth or is discovered during the first year of life Paraplegic rigidity may possibly be confused with other forms of para plegia and especially with that resulting from spinal caries Certain cases of pontine tumour may closely resemble generalised rigidity The occurrence of such conditions during the first 2 years of life is however very rare

Prognosis —In many cases of generalised rigidity and in all cases of paraplegic rigidity there is a tendency to slow amelioration of the rigidity an increase of volun tary power and control of the muscles in the course of time especially under the in fluence of careful training and in paraplegic rigidity if the mental acuity be not seriously impaired laborious treatment may result in an almost normal condition of the limbs by the age of puberty On the other hand some cases of generalised rigidity become progressively worse and succumb usually before the end of the fourth year Bilateral athetosis and choreic diplegia as a rule follow a very slowly progressive course without tendency to a fatal result Paraplegic rigidity apart a great many of the cases of all forms of diplegia succumb before the sixth year and in those who survive this age the tenure of life is short few reaching far into the third decade of life

Treatment —In those cases with a marked degree of mental impairment and in those which show a course of progressive degeneration no treatment is of avail In slighter cases of generalised rigidity and in paraplegic rigidity treatment is to be

directed to the prevention of contractures to regaining of voluntary control and the improvement of mental acuity There is perhaps no disease which demands greater patience and persistency in carrying out of suitable treatment and there are few diseases in which more brilliant results may be produced from apparently hopeless cases by pertinacity in treatment It is in the early years when treatment is for the most neglected that good results are more quickly and readily obtained From the first regular massage and passive movements should be employed Voluntary movement should be encouraged as far as possible and as power and movement increase gymnastic exercises of every kind should be employed Rigid apparatus for prevention of deformity and to reduce contracture is harmful for it increases the weight of the limb and interferes with movement, which is the remedy with which paralysis is to be combated Tenotomy is of great service in the relief of deformity and contracture and should be soon followed by passive movements It should never be performed unless a fair degree of voluntary power is present Many of the patients seem to improve more rapidly if thyroid be administered in moderate daily doses

INFANTILE HEMIPLEGIA

While in childhood hemiplegia of slow onset is due to the same causes as in adults cerebral tumour being the common cause yet the majority of the cases of infantile hemiplegia of rapid onset are examples of diseases peculiar to children to which no comparable disease occurs in adults and to such cases the term infantile hemiplegia is restricted These conditions are due to gross organic lesions of the brain and for this reason must be strictly separated from the cerebral diplegias which are the result of cell lesions and not of gross lesions

Ætiology—In two thirds of all the cases the onset occurs within the first 3 years of life The malady becomes increasingly rare as childhood advances A few of the cases are of prenatal origin and a few are due to syphilitic fœtal vascular disease Again a very few cases are due to obstetrical events during birth by which the cerebrum is injured Acute infective diseases play a very important role in the causation of the disease for about one third of all the cases develop the malady during the course of a known infection By far the most important of such fevers are measles and scarlet fever but hemiplegia may occur in the course of pertussis small pox rubella diphtheria dysentery pneumonia typhus typhoid mumps malaria chorea and endocarditis While there can be no doubt that primary vascular lesions are responsible for many of the cases in which this condition complicates the specific fevers (whooping cough for example may cause cerebral hæmorrhage marasmic conditions in any fever may cause thrombosis of cortical veins and chorea and endocarditis may cause embolism) yet in some cases an inflammatory lesion of the brain or encephalitis is present

Pathology—The following lesions are met with either alone or combined in order of frequency (1) Atrophic sclerosis (2) cyst formation (3) shrunken patches resembling wet wash leather with some degree of atrophic sclerosis in their vicinity and (4) porencephaly The general appearance of these lesions which appear to be varying degrees of the same process suggests the end result of a vascular disturbance usually confined to the area of distribution of the middle cerebral artery There is evidence that many of them result from cerebral embolism occurring immediately after birth in association with the closing of the ductus arteriosus

Symptoms—The onset is rapid and in two thirds of all the cases the disease is ushered in by convulsions which may be unilateral but are more frequently general and are frequently repeated during a period of from a few hours to 24 hours after which the patient sinks into a subconscious state from which he gradually emerges in the course of a few days to show the signs of some cerebral defect usually hemi-

plegia sometimes hemianopia or aphasia or any other sign of local cerebral or cerebellar lesion Pyrexia often accompanies the convulsion and vomiting is common The onset may be without convulsions or loss of consciousness

The relation of the onset of the paralysis to the convulsion varies It may reach its height immediately after the initial convulsion or slight hemiparesis may occur which deepens after each subsequent convulsion Sometimes the early convulsions leave no paralysis but this appears towards the end of the first week either suddenly with fresh convulsion or gradually as the patient recovers from the comatose state The paralysis at its onset is flaccid and involves the whole of one side of the body to a greater or smaller extent An initial monoplegia is of extreme rarity The paralysis may not reach the greatest intensity until the end of the second week Subsequently it lessens in some cases disappearing completely in from a few weeks to 3 months in others it may show no sign of improvement The limbs at first flaccid subsequently become spastic and develop contractures In the course of years there may be great arrest of growth on the affected side and this is not necessarily proportional to the degree of paralysis but apparently depends upon the degree of destruction which has occurred in the parietal lobule Post hemiplegic spontaneous movements of an athetoid choreic or irregular kind are common and are attributable to lesions in the corpus striatum and subthalamic grey matter for which regions encephalitis shows an especial predilection Epileptic fits recur at varying intervals in about half of all cases of infantile hemiplegia These always commence upon the affected side and are sometimes confined to it Mental deficiency is met with in all degrees in relation to the position and extent of the cerebral cortex which is involved in the lesion

Diagnosis—The nature of the malady at the onset with convulsions may possibly be suggested by prodromal pyrexia by the severity and long duration of the convulsions and by the prolonged subconscious state that often follows Convulsions occurring several days after the onset of specific fevers should strongly suggest *the diagnosis When the signs of hemiplegia or of other local cerebral lesions appear* the diagnosis presents no difficulty

Course and Prognosis—In a very small proportion of the cases the patient does not survive the initial manifestations of the disease and dies in convulsions Apart from this event infantile hemiplegia has little tendency to destroy life The initial flaccid hemiplegia tends to improve and gives place to a slowly improving spastic hemiplegia which with the return of some power shows perversity of movement stiffness and slowness ataxy athetosis and choreic movements or tremors according to the position of the lesion The spontaneous movements appear within a year of the onset Slow improvement may go on for years but cases with much mental reduction or in which recurring epilepsy is frequent improve but little

Treatment—We know of no measures that avail to prevent the occurrence or lessen the severity of the cerebral destruction which occurs in these cases Too often the damage to the brain has happened as soon as a diagnosis is possible When the paralysis has developed treatment is to be directed to the prevention of rigidity and contractures by regular passive movements to regaining voluntary control by encouragement and patient exercises and to the improvement of mental acuity Where there is much contracture and deformity tenotomies are of great service provided there be some voluntary power in the muscles the tendons of which are to be divided Recurring convulsions should be treated as idiopathic epilepsy

Severe cases of this disorder as they reach childhood and adolescence present a very characteristic picture The infantile hemiplegia is associated with some degree of failure of growth in the affected limbs and with perverse movements In addition epileptic fits mental retardation and violent temper tantrums are characteristic

Such cases have of recent years been increasingly treated by complete surgical removal of the damaged hemisphere This hemispherectomy is usually followed

not only by cessation or improvement in the fits but by a marked improvement in the mental enfeeblement and the temper tantrums Even more surprisingly the *severity of the hemiplegia instead of being increased is diminished*

PAROXYSMAL DISORDERS OF THE CENTRAL NERVOUS SYSTEM

EPILEPSY

INTRODUCTION —Epilepsy in the widest sense may be defined as a persistent liability to occasional seizures The seizures may be associated with organic disease of the brain or a toxic state and if so the epilepsy is said to be symptomatic If the attacks are of such a nature that they point to a focal lesion of the brain (see p 1497) and particularly if consciousness is retained during the whole or a considerable part of the seizure the term Jacksonian epilepsy is applied to them More commonly there is no discoverable organic disease of the brain and no toxic state (*e g* uræmia eclampsia) with which fits are known to be associated and the epilepsy is then described as idiopathic or essential It is becoming more and more common to restrict the use of the general term epilepsy to this last variety, but it is apparent that the clinical division of the cases of epilepsy into symptomatic and idiopathic cannot be absolute if only for the reason that organic cerebral disease may not declare *itself except by the occurrence of fits In the absence of other indications of cerebral* disease there is no positive feature by which either variety can be recognised

SYMPTOMATIC EPILEPSY

The known causes of symptomatic epilepsy are numerous In addition the diagnosis is often based on assumption because some item in the history of the case provides a basis for supposing that organic cerebral disease or injury has occurred and it requires much knowledge and good judgement to assess whether such an assumption is well founded Injury of the brain of any nature whatever whether from violence from without or from disease within may cause epilepsy Cerebral tumours agenesia encephalitis meningitis cerebral syphilis abscess and certain types of vascular lesions give a high percentage of epileptic sequelæ or accompaniment Another cause of symptomatic epilepsy that should be borne in mind when a previously normal person who has lived abroad develops fits is cysticercosis of the brain Acute intoxications with lead alcohol absinthe and many other poisons may *evoke epileptiform fits as may also eclampsia uræmia hyperpiesis* cholæmia and the specific fevers of childhood and although in these conditions the epileptic phenomena do not usually recur after the intoxication has terminated nevertheless any one of them may be the apparent beginning of persistently recurring epilepsy

IDIOPATHIC EPILEPSY

Definition —A liability to fits or minor seizures prone *to recur over long periods* of time or even throughout life without any discoverable organic disease of the brain or other known cause of fits

The fit is a *disturbance of function due to a sudden* excessive and uncontrolled discharge of nervous centres and this is believed to be due to a disturbance of the metabolism of the cells in which the abnormal discharge originates Of the nature of this metabolic disturbance we are still ignorant and as far as we know it is not associ-

ated with any recognisable change in the histological appearances of the cells concerned The metabolism of nerve cells in activity is accompanied by changes of electric potential and under suitable circumstances the potential changes in the cerebral cortex can be recorded by the electro encephalogram Normally they are rhythmical alternations at the rate of 8 to 12 per second (the α rhythm) and the best records of them are obtained from the occipital region of the head when the patient closes his eyes and relaxes At the time of an epileptic fit there are repetitive excessive electric discharges all over the cortex and these are followed by a period of electrical inactivity lasting some minutes At the time of a *petit mal* attack the E E G shows a single spike indicating one excessive discharge occurring all over the cortex or a succession of spikes In many epileptic patients the electrical record indicates that intermittent abnormalities of the rhythm are present during the intervals between the

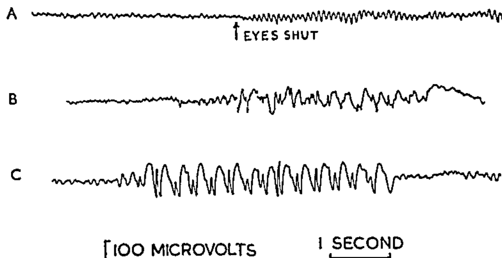


FIG 2 ELECTRO ENCEPHALOGRAMS

A Normal alpha rhythm largely absent with the eyes open and appearing when they are closed 11 cycles per second
B An episode of waves of mixed frequency in a case of idiopathic epilepsy
C An outburst of spike and wave complexes at 3 cycles per second accompanying a *petit mal* attack

By the kindness of Dr W A Cobb

fits and some of them are similar to those associated with a fit *i e* they are sub clinical attacks Abnormalities of the rhythm of potential variation are present in many other conditions besides epilepsy but when the complex known as the spike and wave appears on the record it is believed to be indicative of epilepsy Many epileptic patients however do not show this abnormality on their records and the records may either be quite normal or may show other non characteristic abnormalities Electrical abnormalities are found alike in idiopathic and in symptomatic epilepsy but in the former they are more constantly present and are in general more widely diffused over the cortex and more readily modified by such activities as over breathing

Ætiology—It is important to be clear in our minds what we mean by the cause of epilepsy In symptomatic epilepsy organic disease of the brain is usually present but in idiopathic epilepsy there is no organic disease with which the liability to fits can be associated moreover the same organic disease *e g* a glioma of one frontal

lobe may be associated with fits in one case and not in others It is thus evident that the organic disease is not the immediate cause of the liability to abnormal dis charges but it is a more remote cause Of the more immediate cause (or causes) of the liability to attacks almost nothing is known beyond the indications of metabolic disturbance in nerve cells that have already been referred to Of remote causes of the liability in addition to organic disease of the brain *heredity* is the most important. While this factor is regarded much less seriously now than formerly the fact remains that in a still considerable proportion of cases, a history of epilepsy in a near relative is obtained Moreover recent electro encephalographic observations by Lennox suggest that in the parents (one or both) of epileptic subjects abnormally wide fluctua tions in the rhythm of the brain potentials are unduly common and it may be that while epilepsy as such is not inherited some instability of cortical cell function may be inherited which in combination with other factors leads to the appearance of epilepsy under certain (as yet unknown) circumstances

In the vast majority of cases of idiopathic epilepsy the tendency to fits first reveals itself in childhood or adolescence In 70 per cent. of cases attacks have begun by the age of 20 and in 85 per cent by the age of 25 In a small number of cases idiopathic epilepsy first manifests itself in the fourth or fifth decade but far more frequently fits coming on after the age of 25 are symptomatic of organic cerebral disease Often children starting to have fits in adolescence have had convul sions in infancy

The frequency of fits in the same patient is subject to great variability so that the liability to abnormal discharge evidently fluctuates When it is sufficiently great, there must also be a final exciting cause which starts off the attack—especially the major fit Of the cause(s) of fluctuations in the liability to attacks and of the exciting causes of fits we are again quite ignorant The most that can be said is that some thing is known from empirical observation of the conditions in which fits often occur These are subject to great variability from patient to patient but often show great uniformity for the same individual

More than half of all (convulsive) attacks occur during sleep There are many individual patients whose attacks invariably occur during sleep and this is often called nocturnal epilepsy but the liability attaches to sleep whether nocturnal or diurnal and the Sunday afternoon nap in front of the fire is frequently productive of fits in such patients Of the nocturnal fits many occur soon after the patient has fallen asleep, but still more in the last few hours before waking There are some epileptics who never have fits except in sleep and in general the liability to fits during sleep is much greater than during the waking state The next greatest frequency of attacks attaches to the first hour or so after waking Many patients have their attacks usually or invariably when washing in the morning or dressing or about breakfast time, so much so that for the average patient the liability during this first waking hour seems considerably greater than for any other hour of the twenty four During the rest of the day the liability to attacks for the average patient is much less but this is not to say that many fits do not occur during the day and occur sometimes under the most unpredictable circumstances In general the patient seems less liable to attacks while intent on the day s activities than when inactive relaxed or lounging or dozing In the evening especially in the last hour before bedtime the average liability to fits is again increased and some patients usually have their attacks at this time but in general the evening liability is not nearly as great as that of the first morning hour

In women there is a pronounced increase of liability to fits in association with the menstrual period beginning about 5 days before the onset of menstruation and lasting till the end of 48 hours after its termination with its maximum in the 2 days preceding the menses In many women who are relatively mild cases of epilepsy the attacks occur only at such times

There is a popular idea that emotional excitement has an influence in precipitating fits in epileptic patients but it is rarely that the personal histories of patients provide any confirmatory evidence for this and the only emotion that seems to have any effect in increasing the liability to attacks is fear and even that is doubtful In a few patients concentration on studies has an adverse effect

Physical disturbances such as vertigo nausea vomiting seem also to increase the liability to fits as also does physical injury General anæsthetics often precipitate fits in epileptic subjects and an injection of novocain seems to increase the liability so that an attack may occur after some hours

The retention of water in the body brought about by the intake of a large amount of fluid and the injection of pituitrin subcutaneously leads to the occurrence of a fit in 50 per cent or more of susceptible subjects and this has been used as a diagnostic test for epilepsy but such a test is rarely called for if adequate attention is given to the description and circumstances of suspected fits

Symptoms —PRODROMATA —The circumstances which immediately precede the occurrence of an attack are of some importance As has been mentioned it is uncommon speaking generally for an attack to occur when the attention is fixed or when some act is being performed and from this it follows that the epileptic is relatively or absolutely free from attacks when at work and doing and only in rare cases comes to harm or injury from accident Some patients are able by effort of will in fixing attention or by the performance of some vigorous action to arrest attacks which threaten or have even begun

Sometimes a change in the general condition of the patient may make him aware or may acquaint those around him that an attack is pending and such signs of altered health may herald an attack for from a couple of hours to a week Headache irritability restlessness euphoria depression lethargy somnolence unusual appetite and a peculiar vacant look may all be met with in this connection

Not infrequently the attack is preceded by paroxysmal manifestations which are in reality minute attacks such as partial lapses in consciousness a sense of strangeness dreamy state jactitations of any of the muscles exactly resembling those seen in uræmia, slight auras giddiness sneezing and yawning

DESCRIPTION OF THE ATTACKS —The varieties of the epileptic attack are legion and several types may occur in the same subject—indeed it is unusual for fits to be always of the same type in one subject They tend to vary both in degree and nature They are usually divided into major attacks in which spasm is conspicuous and the less spectacular minor attacks in which spasm is not a prominent feature This distinction is purely artificial for most patients have attacks of both varieties and the two merge by insensible gradations the one into the other

The following description will serve to illustrate the more definite manifestation of epileptic attacks

GENERAL CONVULSIVE FITS (*haut* or *grand mal*) —There is some reason for believing that every major attack has a local commencement in some region of the brain and that it is in reality a local fit which rapidly becomes general When such an attack commences with a local aura there is proof positive of local commencement When it commences with conjugate deviation of head and eyes to one side this is a certain indication that the disturbance commences in the opposite hemisphere When the spread of the disturbance is so rapid as to cause instant loss of consciousness there is no memory to retain the initial event of the attack The seizure may begin with any of the local manifestations described later the epigastric aura and giddiness being two of the most frequent Or the patient may only be aware of his attacks from the condition in which he finds himself after their occurrence The tonic spasm commences with conjugate deviation of both eyes to one side followed by rotation of the head to the same side The blood pressure falls the countenance is for a moment pallid the eyes widely open the pupils dilated the corneæ insensitive The march

of the tonic spasm usually causes head retraction and opisthotonos the upper extremities are stiff in flexion and adduction the lower extremities in extension If standing the patient falls usually backwards but the conjugate deviation of head and eyes may bring his face to the ground first The respiratory muscles and larynx going into spasm produce the epileptic "cry" and the respiratory movements being no longer possible the face darkens with the asphyxia and the sphincters may relax with the evacuation of bowel or bladder The protrusor spasm of the tongue and the closing spasm of the jaw may cause the tongue to be bitten After the tonic spasm has lasted some seconds and perhaps has produced such a degree of asphyxia as seems hardly compatible with survival it begins to break into a series of sudden shock like, jerky movements—the clonic spasm—which continue for some seconds becoming less regular and occurring at longer intervals until with a final jerk the muscles become perfectly limp Meanwhile the relaxation of the respiratory and laryngeal spasm has allowed the respiratory movements to return and to churn up the saliva often bloodstained which escapes at the nose and mouth in the form of froth At the end of the attack there is complete and unrousable loss of consciousness, the pupils are dilated and insensitive to light the corneal reflexes absent the knee jerks absent and the plantar reflexes extensor in type In a short time the knee jerks return the plantar reflexes return to the normal and consciousness returns Usually the patient is dazed feels ill, has marked headache and if left to himself soon sleeps heavily for some hours It must be noted that the general convulsive attack almost always leaves the patient face downwards so that he has been known to drown in a puddle an inch deep and has been asphyxiated by his own pillow The latter event is by far the commonest way in which the epileptic meets his death from accident in a fit

The epileptic cry—There are two quite different sounds that may occur at the commencement of an epileptic attack The one is a natural conscious cry of terror at the advent as in the patient who alternated piercing screams with ' It is coming! It is coming! before the convulsion commenced It is curious how rarely any memory of such cries or utterances remains with the patient The other is the epileptic cry proper—a weird unearthly hollow sound produced by inspiratory spasm drawing air over the nearly closed vocal cords This cry occurs in a minority even of severe cases for the obvious reason that it is determined by a particular march of the spasm If the inspiratory spasm occurs before the larynx has gone into spasm or after it is in spasm there can be no laryngeal noise but only the commonly witnessed pharyngeal and buccal grunting and gurgling The spasm must be so timed that the inspiratory spasm must occur as the larynx is closing and this only obtains in a minority of the cases

Tongue biting—Some patients always bite the tongue others never and some now and again The tongue is always bitten at the side and some way from the tip because it is deviated to one side in the spasm and its thicker part brought between the molar teeth The same side is usually bitten The tongue cannot be bitten unless protrusor spasm occurs either before the jaw has gone into tonic spasm or after it has broken into clonic spasm If any other march of spasm occurs the tongue escapes It is remarkable how little scarring occurs even from severe and repeated tongue biting unless a piece is bitten clean out

Incontinence—Though common incontinence is by no means invariable even in severe attacks More often it is the urine alone that is evacuated much more seldom the bowel alone still more rarely both A rare phenomenon during an epileptic fit is seminal emission

Secondary events—The degree of asphyxia during the attack may be severe and blood vessels may give way under the stress with the production of surface ecchymoses or deep hæmorrhages including cerebral hæmorrhage The spasm is powerful and may give rise to much subsequent aching as if the patient had been beaten all

over It may dislocate joints rupture muscles and even break bones A dislocation once produced in a fit is very liable to recur with subsequent fits

Duration of epileptic attacks—Two minutes may be given as an outside time limit for the duration of an individual attack from its commencement to the end of the active phenomena and in convulsive attacks to the end of the spasm Usually the time is much shorter than this and often is a few seconds only Sometimes attacks are described as of much longer duration When analysed such attacks will be found to be a series of attacks with very short intervals or slight attacks with post epileptic functional spasm or hysterical attacks

Other varieties of convulsive disorder are commonly encountered either as heralds of a *grand mal* attack or as the sole expression of the epileptic disturbance

SIMPLE JACTITATION—Simple twitchings of individual muscles or groups of muscles occurring now in one part of the body now in another are seen in the majority of epileptics at some time or other They are conspicuous in the convulsions of childhood where they often constitute the chief clinical feature They are well known as the carphology or subsultus tendinium of uræmic and eclamptic attacks, and in the typhoid state They may be not infrequently noticed in the epileptic person when he is otherwise well and engaged perhaps in conversation or other occupation Gowers emphasised epileptic twitching as a prodroma of an oncoming severe attack but while in some instances this is undoubtedly true yet it frequently occurs when no attack follows It has been called epileptic myoclonus'

LOCAL FITS—First studied by Hughlings Jackson these events bear the name of Jacksonian epilepsy and this term has unfortunately become coupled with common errors that were no part of Jackson s teaching These are (1) that some local disease invariably underlies the Jacksonian fit and (2) that the Jacksonian fit necessarily consists of local motor convulsion Actually in many cases naked eye and micro scopic examination may fail to reveal any local lesion and none such may be present Also the Jacksonian fit may consist of phenomena involving any possible cortical function It may be added that local disease of the brain quite commonly evokes generalised fits indistinguishable from those of idiopathic epilepsy and conversely that the latter form of epilep y may express itself in the form of Jacksonian fits

In local convulsive attacks the common foci of onset are the angle of the mouth the thumb and index finger and the great toe but the spasm may occasionally begin elsewhere It rarely produces conjugate deviation of the eyes as a primary move ment but usually in association with and secondary to deviation of the head The convulsive movements may remain confined to their place of onset throughout the fit or may spread widely so as to involve a whole limb one half of the body or the entire musculature In fits involving the musculature of the right half of the face and tongue speech is usually lost during the attack and returns shortly after its cessation Spasm never affects the muscles of one eyeball alone but the spasm is in terms of conjugate deviation of both eyeballs in one direction The same rule applies when the neck is affected for the head is then either rotated to one side or extended or flexed on the chest With the other bilaterally associated muscles it is different for the tongue is affected on one side only as is also the face The onset is with tonic spasm which after a little while gives place to broken or clonic spasm becoming more and more intermittent and finally ceasing In some cases but by no means in all the convulsion leaves varying degrees of weakness in the affected muscles—Todd s paralysis or post epileptic paralysis—with transient signs of loss of function of the pyramidal system such as loss of trunk reflexes increase of jerks and extensor plantar reflexes

Epileptic spasm usually puts the hand in the position of extension at the inter phalangeal joints and flexion at the metacarpo phalangeal joints with flexion at wrist and elbow and adduction at the shoulder The feet are dropped and inturned with extension at the knee and hip Usually the trunk is in opisthotonos

The sequence of tonic spasm followed by clonic spasm, though usual in epilepsy is not invariable Purely tonic fits may occur with no clonic spasm the tonic spasm remitting suddenly Such fits are usually of slight severity and duration On the other hand the spasm may be clonic only The simple jactitation already described may be taken as a simple clonic fit Local fits especially of the face and of the hand may be purely clonic

Loss of consciousness in local fits—This seems to depend upon the extent of the cortex involved With narrowly confined fits there may be no evident impairment at all as in local convulsion of the face or hand or as in a patient who vividly described a slow visual fit as it was occurring When the fit spreads consciousness is usually impaired, and when lost, it is lost late in the fit For example it is usual for a convulsion which spreads to one half of the body to cause some impairment and if it involves both sides generally consciousness is always lost

LOCAL PARALYTIC FITS (*simple paralysis*)—This is the rarest of all forms of the epileptic attack It consists in a sudden inability relative or complete, to use a limb or one side of the body or the whole voluntary musculature, with no preceding convulsion There are the usual signs of cerebral paralysis—at first flaccidity with a tendency for the jerks to fail a few moments later increased jerks, with absent trunk reflexes and extensor plantar reflexes all of which signs soon disappear The attack may occur as an isolated phenomenon More often a slight ' minor " attack or a local sensory attack accompanies the onset of the paralysis Sometimes such an attack may result from local disease of the brain Such episodes when involving the right face or right side of the body may occasion aphasia, or the aphasia may occur alone as the attack of simple paralysis Such attacks of simple paralysis without convulsion are well known in uræmia hyperpiesia and general paralysis of the insane

SENSORY EPILEPTIC DISTURBANCES—Numerous sudden sensory disturbances may be met with in epilepsy They may be related to the organs of special sense to those of common sensibility or to those of visceral sensibility They may occur as isolated events and so constitute the whole epileptic attack Often however the disturbance of the cortex spreads widely, involving general convulsion and loss of consciousness but the initial phenomena are remembered by the patient as the ' warning of the attack and have from ancient times been termed auras when preceding general convulsion In reality they constitute an essential part of the attack as showing the region of the brain in which the disturbance starts and in every patient who has such warnings preceding his severe attacks the warnings occur at times by themselves without any such sequel

Visual fits—These may take the form of negative phenomena such as dimness of vision complete darkness or hemianopia or of positive effects such as flashes of light scintillating stars or balls of fire or of both together in the form of blindness with flashes of light In the last case they may closely resemble the visual phenomena of migraine and are not infrequently caused by a local lesion of the occipital region Complex visual hallucinations may occur

Auditory fits—The hallucinations of sound may be of any nature—hissing booming and elaborate musical sensations as of bells being common There is usually a sense of coincident deafness of far away hearing which passes off with or soon after the sound

Olfactory and gustatory fits—These hallucinations are always described as of ' flavour usually unpleasant Very often movements of the lips tongue and jaw or swallowing movements are present and the dreamy state referred to below may be associated From the location of the functions of smell and taste in the cortex of the uncinate gyri and from the common occurrence of fits of this character in lesions of these convolutions this type of fit is often referred to as the uncinate fit

Sensory fits—These hallucinations may have their seat of commencement in any part of the body They may remain local but more commonly they spread from the point of origin in terms of the local representations of the body in the cerebral cortex and usually from the periphery towards the trunk and head but a sensory fit may spread to the extreme periphery first For example commencing in the fingers it may spread up the arm to the head or on reaching the shoulder it may invade trunk and leg before ascending to the head It may be bilateral and may be confined to the anterior or posterior aspect of the body

The sensation may be described as ' numbness , tingling pins and needles vibration , 'rushing' as if the limb were withering , much more rarely actual pain Sometimes the sensation is indescribable The sensory attacks have their origin in a local disturbance of the parietal region of the cortex and may indicate the presence of an organic lesion in that region They may be accompanied or followed by temporary loss of sensibility in the form of astereognosis, loss of sense of position or anæsthesia

Another group of sensory fits for which it is impossible to give any definite cerebral localisation at present is that of the so called visceral auras which are mainly referred to the distribution of the vagus nerve Such are the very commonly occurring epigastric sensation and sensations of choking dyspnœa nausea and cardiac sensations

Disturbances in the realm of the vestibular nerve are common indications of epilepsy Sudden giddiness may be the sole indication of epilepsy and is a common initial event in major attacks It may be indicative of the sudden fall of blood pressure or the feeling of rotation may be consequent upon early spasm causing conjugate deviation of the eyes

PSYCHO MOTOR FITS—These may take the form of peculiar mental states of instantaneous onset remembered afterwards sometimes in exquisite detail some times only in vague character Emotional conditions of fear or horror which may cause the patient to attempt with violence to escape from his surroundings— cur sive epilepsy—may occur Or the attacks may take the form of a sudden feeling of misery or an intense sense of personal wrongdoing a sense of intense familiarity in surroundings which are unfamiliar a sudden sense of strangeness as in a patient whose fit was suddenly seeming to be somewhere else a sense of euphoria or of intense mental energy a dreamy state often associated with smacking of the lips and champing or swallowing movements which often has a pleasurable emotional tone Again the psychic fit may take the form of a highly complex and detailed hallucination Other psycho motor attacks may express themselves as outbursts of uncontrollable rage and in rare instances the patients make attacks of great ferocity on unoffending individuals and have no recollection of these incidents afterwards

MINOR EPILEPSY (*petit mal*)—The disturbances to which this term is given show considerable variation in degree but share in common the fact that there is a sudden impairment or loss of consciousness

Simple loss of consciousness—In this the commonest of all minor phenomena there is a simple break in the continuity of consciousness The train of thought and action is suddenly arrested for a few seconds and there is a sudden stillness of posture and facial expression which attracts the attention of a witness The face may show sudden pallor a vacant expression and curious fixity of the eyes with large pupils The patient does not fall or move or drop anything that he is holding In a few seconds the attack is over leaving the patient unable to describe what has happened perhaps a little confused for some seconds sometimes emotional and even hysterical More often he continues what he was about as if nothing had happened Such attacks sometimes occur very frequently even hundreds in a day

Simple loss of consciousness with falling—The patient suddenly falls without warn ing in the extended position and almost always prone so that his head reaches the

ground first and his forehead receives the bruise He regains consciousness immediately and picks himself up as if nothing had happened In another form of this type the head or the head and trunk alone are affected the patient does not fall but simply drops the head forward

Simple loss of consciousness with slight spasm —This forms a gradation from the above types to the definitely convulsive seizures The spasm is seen as conjugate deviation of the eyes, and perhaps of the head also, or it takes the form of laryngeal and respiratory action giving rise to a groaning noise or it may involve any part of the musculature

CONDITION AFTER ATTACKS —The epileptic fit may leave no after effects whatever even though it be severe but this is unusual On the other hand even the slightest attacks may cause conspicuous sequels Sleep and headache are very common especially following convulsive attacks and they may be alternative effects in that if sleep occur there is no headache, but if it be prevented there is severe headache The post epileptic paralysis of Todd has already been described and also the aphasia which may follow right sided attacks The mental state is usually affected by the attack, and returns to the normal sometimes quickly sometimes slowly Commonly the patient is dull and dazed speaking at random, unreceptive, irritable and does not fully recognise his surroundings Many patients especially women weep During this state of impaired consciousness the patient may pass into a condition of mental automatism in which various acts are performed in a conscious manner but of which no recollection is afterwards retained One patient always prepared for bed after her minor attacks, and on one occasion proceeded to undress in the stalls of a theatre The acts performed during post epileptic automatism may have no relation to the life and mentality of the patient He may do spiteful and criminal acts to those he dislikes This fact has an important bearing as regards the criminal responsibility of the epileptic These post epileptic conditions occur commonly after minor attacks but they may also occur after major fits they seldom occur when convulsion has been severe

Vomiting may occur after any type of epileptic fit but it is most often met with after a convulsive attack As it occurs during the period of unconsciousness there is some danger of the vomited material being drawn into the larynx Though Gowers mentions a case in which this event proved fatal accidents of this nature are exceedingly rare

MENTAL DETERIORATION AND ABERRATION IN EPILEPSY —Many epileptics especially those who have frequent attacks show signs of mental deterioration which is often progressive and which may become severe and end in chronic insanity while others show no such mental troubles and some of these fulfil a long life with the highest standard of capacity

There seems to be no correlation between the type of epilepsy and mental degeneration though the latter is widely held to be more frequent and more severe when many minor attacks occur

The tendency to mental failure is greatest in the cases which commence in childhood and lessens as age increases but in the epilepsy commencing in the degenerative period of later life the incidence again increases In its slighter form there is merely defect of memory of attention and power of acquisition In more severe degree there is greater imperfection of intellectual power weakened capacity for attention and often defective moral control Mischievous restlessness and irritability may develop into vicious and criminal tendencies with advancing age Every grade of intellectual defect may be met with to actual imbecility Paroxysmal outbursts of mental derangement may occur sometimes transient and immediately following a fit sometimes without a fit and sometimes lasting for weeks or months

PERIODICITY —While some patients may have fits at any time and at all times yet there is a tendency in the majority for the attacks to occur at particular epochs

and not at others Epilepsy may be strictly ' nocturnal ' or diurnal ' It may occur only on rising in the morning or solely at the menstrual epoch The fits may come in batches of several in one day at intervals of many months A knowledge of the periodicity when present is of great value in the successful treatment of epilepsy

SPECIAL VARIETIES OF EPILEPSY

EPILEPSY FROM LOCAL DISEASE OF THE BRAIN —Almost any lesion of the cerebral hemispheres may produce symptomatic epilepsy But not more than 5 per cent of all such lesions do this The convulsions which may occur in cerebral thrombosis encephalitis and meningitis are examples of epilepsy incident with the onset of an acute lesion Lesions of the brain in childhood seem to be more commonly associated with epilepsy than when occurring in adult life Agenetic states of the brain of prenatal origin (cerebral diplegias) are associated with epilepsy in 30 per cent of the cases and infantile hemiplegia is followed by epilepsy in about the same proportion In adults the commonest causes of symptomatic epilepsy are supra tentorial tumours and cerebral syphilis Increased intracranial pressure by itself as for example in subtentorial tumours seldom if ever, produce fits unless there is associated involve ment of the hemispheres as occurs in meningitis subarachnoid hæmorrhage or hemi sphere tumours Cerebral abscess situated in the hemispheres not uncommonly produces fits

The fits caused by local lesions may be in every respect identical with and in distinguishable from the usual type of epileptic manifestation from the slightest momentary minor fit all through the local sensory and motor fits to the severe general convulsion of instantaneous onset and immediate loss of consciousness There are the same auras and the same sequels It may perhaps be said with relative truth that the splanchnic auras (epigastric cardiac etc) are uncommon and that there is a greater tendency for consciousness to be lost late

The minor attack is the least common fit occurring as the result of a local lesion the general convulsion by far the most common while the local fit holds an inter mediate position and its nature is often indicative of the position of the lesion

TRAUMATIC EPILEPSY —Special reference may be made to one of the examples of epilepsy caused by organic cerebral change namely trauma on account of the increasing incidence of head injury both in civilian life and as a result of war It is generally accepted that the underlying pathological change in traumatic epilepsy is the development of a cortical cicatrix although the occurrence or otherwise of epilepsy following such scar formation will be largely determined by the degree of stability of the particular brain affected

The incidence of traumatic epilepsy is variously estimated by different writers but it is agreed that the incidence is much higher in penetrating than in closed injuries of the brain In the case of closed injuries of all severity the estimates range from 4 per cent to 8 per cent the liability increasing with the severity of the injury as judged by the duration of unconsciousness In penetrating wounds of the brain estimates vary from 10 per cent to 25 per cent and Symonds suggests that 15 per cent represents the approximate incidence The development of epilepsy character istically follows a considerable latent interval which varies from a few months to many years and averages 2 to 3 years

In another group of cases however the fits seem to coincide with the process of healing the attacks beginning within a month or two of the injury and ceasing after 1½ or 2 years

Any form of epileptic disturbance may follow trauma but the generalised convul sion is the most common and it is not infrequently associated with typical attacks of *petit mal*

PYKNOLEPSY —This is a *form occurring in children, so called* because of the great number of the fits which may occur daily These are of the slight minor type any sign of spasm being infrequent It is rare for any major fit to occur There is no mental impairment whatever no deterioration of health and no result is obtained by any *form* of treatment The malady invariably ends in spontaneous cure usually before or at the age of puberty Its separation from minor epilepsy is of uncertain validity

CARDIAC EPILEPSY —This is a convenient term for the epilepsy which occurs in Adams Stokes' disease and in paroxysmal tachycardia and for the fits which may occur in congenital heart disease and in some forms of cyanosis They are probably related to sudden cerebral anoxia

VASO VAGAL ATTACKS —Under this misleading title Gowers described a recurrent paroxysmal symptom complex with some or all of the following components a sensation of fullness in the epigastrium, præcordial pain or discomfort, difficulty in breathing a sense of impending death a slowness of mental operations but without disturbance of consciousness, a sense of physical fatigue and coldness of face and extremities These symptoms wax and then wane gradually and may be present for as long as 4 hours from onset to disappearance

Gowers stated that he used the term " vaso vagal as a purely descriptive one but without *implying any theory of causation Unfortunately those who have adopted* his terminology have overlooked its lack of foundation The term has no precise meaning no sound basis of observation and no proper place in neurological terminology

MYOCLONUS EPILEPSY —In this group are included (1) Epilepsy *of an ordinary* type in which there is much epileptic jactitation of the muscles between the fits (2) cases of Unverricht s myoclonus in which epilepsy is coincident

REFLEX EPILEPSY —Numerous cases are on record in which fits could be produced with great regularity by certain specific stimuli To these the term reflex epilepsy has been applied The most frequent of such exciting causes is some tactile stimulus to a particular part of the body especially when unexpected In another form the stimulus may be a sudden noise or music Other cases are precipitated by emotion

EPILEPSIA PARTIALIS CONTINUA (*focal status epilepticus*) —Under this name have been described cases of focal epilepsy usually consisting of clonic spasm which remain confined to the part of the body in which they originate but which persist *with little or no intermission for hours or days at a stretch*

This form of epileptic discharge is most often seen in the face and is probably always associated with local organic disease of the corresponding area of the cerebral cortex

STATUS EPILEPTICUS —In this condition severe convulsion succeeds severe convulsion at short intervals without any return of consciousness during these intervals It is as if convulsion recurred as soon as the body recovered sufficiently from the exhaustion produced by the last convulsion Meanwhile the temperature rises and may reach a hyperpyrexia The difficulty in feeding and providing fluids the severe muscular exertion and the pyrexia add their dangers to those of exhaustion and the patient is very apt to succumb—usually to a terminal broncho pneumonia Status epilepticus must not be confused with frequently recurring fits in which there is some return to consciousness during the intervals though it frequently develops from such a condition for the latter is not accompanied by a rising temperature the fits are more readily subdued, and are not of nearly so severe a prognostic import If the convulsions of status epilepticus cannot be stopped by treatment the patient usually dies from sudden collapse or the first ceasing he remains delirious for a while with rapid heart and high temperature and dies of broncho pneumonia *Status* epilepticus may be met with in acute lesions of the brain and in chronic lesions such as general paralysis of the insane It may occur in acute poisoning with lead bismuth

and absinthe It may develop suddenly in any type of epilepsy whatsoever sometimes without apparent cause sometimes as the result of over exertion and excitement sometimes when medicines which have been regularly administered and which have kept the fits in check are suddenly cut off

Diagnosis—The recognition of epilepsy requires a working acquaintance with the nature of its many manifestations and especially of the slight forms little exterior ised which may be easily overlooked or misinterpreted The sudden unexpected onset without cause the transiency, the recurrence and the circumstances of the moment are useful aids If all these clinical features are taken into account a con fident diagnosis can almost invariably be made Epilepsy (idiopathic or symptomatic) is the only condition which causes attacks in sleep with the exception of the nightmare and the latter seldom causes difficulty in diagnosis Again if an attack occurs soon after waking there is a very strong presumption that it is epileptic The electroencephalogram is seldom helpful in the primary diagnosis but may give useful indications in the differentiation between idiopathic and symptomatic varieties The water-retention test, which seeks to provoke a fit for diagnostic purposes is rarely justifiable unless malingering is strongly suspected

Syncopal attacks (rapid lowering of blood pressure) can often be distinguished from epilepsy by their slow onset, the gradually increasing pallor or greyness the distancing of sound the nausea and flatulence the presence of an obvious cause their duration and the absence of any convulsive element

The hysterical attack has to be distinguished from the convulsion of epilepsy Hysterical convulsion has not the manner nor the march of epileptic spasm It never begins with conjugate deviation of head and eyes to one side there is not the orderly spread of convulsion and there is never anything but a poor imitation of the sequence of tonic followed by clonic spasms The movements in the hysterical fit are purposive spectacular violent and are liable to be increased by restraint and are rapidly abolished by complete inattention The hysterical fit never occurs except in the presence of an audience for it would then be purposeless and it never occurs during sleep the tongue is never bitten though other parts of the body and other people may be There is no transient abolition of the tendon jerks nor transient appearance of the Babinski plantar response The sphincters are never relaxed Intense converging spasm of the eyes is a common feature of the hysterical attack but this sign is not met with in epilepsy When elaborate disorders of behaviour follow slight and rapidly transient epileptic attacks the distinction between these and purely hysterical attacks is often difficult and sometimes impossible except after long observation for the initial epileptic attack may be practically unnoticeable and the subsequent events may be typical of hysteria and are usually amenable to the same line of treatment Often some point in the circumstances under which the attack occurs will settle the diagnosis Any attack having occurred during sleep or any attack in which the patient has fallen in circumstances of serious danger as among the traffic of a London street or any attack occurring when the patient cannot attract the attention of others establishes the diagnosis of epilepsy The best plan is to regard all fits as possibly epileptic and every fit of doubtful type as probably epileptic until time and circumstance bring definite conviction

Migraine may sometimes closely simulate epilepsy when sudden paralysis or sensory auras or visual hallucinations occur without headache But while the sensory phenomena of migraine may last for 5 to 30 minutes those of epilepsy have a duration of seconds only

Careful search must be made in every case for all the bodily conditions with which symptomatic epilepsy may be associated Papillœdema headache and vomiting may reveal increased intracranial pressure from some lesion of the brain while local paralysis sensory loss visual or other defect may indicate a local lesion of the brain past or present and this may also be suggested by the nature of a local fit. The

presence of rickets infantilism undue adiposity, etc may indicate the presence of some definite metabolic or endocrine disorder Renal function and the condition of the blood pressure should always be examined for even in early infancy fits may be uræmic and in the recurring convulsive attacks associated with chronic nephritis and with cystic renal disease and arterial hypertension the causal disease is frequently unrecognised Where syphilis is likely, the reactions in the blood and cerebrospinal fluid should be examined Lastly any evidence of chronic intoxication by metals, alcohol absinthe etc should be sought for

Cysticercosis epilepsy should be thought of when the patient has lived abroad Diagnosis depends upon the palpation of cysts in the tissues or the shadows in radio graphs of calcified cysts in the muscles, particularly those of the shoulders thighs and calves or within the skull

Prognosis —The outlook in epilepsy is so variable that it is difficult to indicate any but the broadest principles in prognosis Nor can a definite forecast be made in any case until the result of treatment has been watched for some time, for cases apparently favourable may prove rebellious and those apparently most unfavourable may turn out brilliant successes Speaking generally a cheerful outlook is justified in all cases except those in which there is progressive mental deterioration, and in these the outlook is hopeless in proportion to the rapidity of the mental change Naturally, in those cases which are associated with serious bodily disease such as brain tumour renal disease and hypertension the prognosis involves that of the exciting condition

The danger to life from the epileptic attack itself either directly or indirectly is not great However severe the fit it is extremely rare for death to occur and when this happens it is from turning over and smothering with the wetted pillow or by choking from the aspiration of vomited material Injury burning and drowning may cause death yet the number of epileptics who meet their deaths in this way is so infinitely small as almost to remove the danger of accident from practical per spective In the rare status epilepticus however the danger to life may be very great Spontaneous cessation of the attacks occurs in a proportion of cases The convulsive attacks of infancy, which continue for some years after all cause to which they can be attributed has passed away, often cease for ever at the age of 4 to 6 years Again after 20 years of age spontaneous cessation is met with

The probability of cure arrest or amelioration by treatment may be entertained in all cases where no mental deterioration exists and where no insuperable bodily disease determines the epilepsy in proportion as the only method of cure—the securing arrest of the attacks for a considerable time by drug treatment—can be adequately administered over a long period It is greater when periodicity in the occurrence of fits allows these to be anticipated by drug administration It is much greater when the following out of education or the continuance of regular employ ment allows of a fully occupied and satisfying life and much less when education is stopped pleasures and sports forbidden and the patient condemned to social inferiority and ostracism and to a gloomy narrow life of frustration because he has a few fits It is perhaps smallest when severe attacks occur daily or at short intervals and when both major and minor attacks occur in the same subject

Treatment —*General treatment* —The general principles for the maintenance of health if good or for its improvement if poor should be adopted Whenever possible no change whatever should be made from the régime of life of a normal person In childhood education discipline and pleasures and school life should be continued upon strictly normal lines and the adult should continue with work and occupation The life of the epileptic should be as regular as possible and physical and emotional strains changes in occupation and diet should be reduced to a minimum Continuity of treatment is of great importance and any course adopted should be given a thorough trial before being modified Frequent changes of doctor should be

avoided No advantage has accrued from the adoption of special diets such as the prohibition of meat the exclusion of salt or the use of purine free foods though the production of a low grade of acidosis by a ketogenic diet is occasionally of value in the epilepsy of children Alcohol seems to be an excitant of the epileptic attack and should be forbidden

The forbidding of such pastimes as may be fraught with danger should a fit occur, such as swimming boating, cycling and car driving, may be necessary

Marriage and pregnancy —The subject of epilepsy sometimes seeks—but rarely heeds—advice as to the expediency of marriage both in its effects upon himself (or herself) and in respect of any heritable qualities it may possess Marriage has no necessary effect upon the course of epilepsy and as we have seen direct trans mission of the disease is not usual Therefore the sweeping medical prohibitions once so frequent in these circumstances are not in fact warranted by such knowledge as we possess Every case must be considered on its merits It is common though not constant for fits to cease in the epileptic woman when pregnant and in any event the occurrence of fits at this time constitutes no special danger and is not an indication for the artificial termination of pregnancy On the other hand the con firmed and serious epileptic is clearly unlikely to be able to discharge adequately the responsibilities of parenthood

Institutional treatment —In cases where there is low mentality much mental degeneration or insanity and cases with frequent fits where no adequate care and occupation can be provided at home there is every advantage in a colony institution or asylum for epileptics In such patients regular work discipline and interest often mitigate greatly the burden of the malady

Surgical treatment —In the present state of our knowledge surgery has no part to play in the treatment of idiopathic epilepsy Neuro surgical procedures such as encephalography and ventriculography are of great value in establishing or excluding the presence of a space occupying lesion in doubtful cases and in revealing the presence of cortical atrophy porencephaly or ventricular dilatation Such epileptogenic pro-cesses as cerebral tumours or abscesses may be amenable to surgical removal and the epilepsy may be relieved thereby The value of surgery in traumatic epilepsy is more debatable Foerster and Penfield and others have demonstrated the value of the excision of scarred areas of the cortex in selected cases of traumatic epilepsy but demand as criteria for operation that ventriculography should reveal a definite ven-tricular distortion in that area of the brain indicated as the starting point of the dis charge by the nature of the fits and that it should be possible to reproduce an accurate replica of the fit by electrical stimulation of the abnormal area of cortex at the time of operation In many cases of traumatic epilepsy the cortical scarring plays only a precipitating role and there is in addition an inherent instability of the cortex In such cases excision of the scar affords only temporary relief and the fits soon recur in unaltered frequency

Medicinal treatment —Further than the measures above described the treatment of epilepsy is purely medicinal There are now several groups of drugs which have a remarkable effect in arresting or mitigating the occurrence of the attacks in epilepsy They seem to have much the same effect and may conveniently be combined or alternated in the treatment of any given case Sometimes one group is found to suit an individual patient better than the other Moderate doses such as will cause no deterioration in bodily or mental health even if taken regularly and for years seem to bring about the best results

The bromides formerly used universally have been almost completely displaced by the malonyl urea compounds of which phenobarbitone (Luminal) and soluble phenobarbitone are examples These are powerful drugs and must be u ed with care Phenobarbitone has certainly the advantage over soluble phenobarbitone in being more prolonged in its action It is conveniently prescribed in doses of gr $\frac{1}{8}$ to $\frac{1}{2}$

to a child and gr ¼ with a maximum dose of gr 1½ three times in the day to an adult. In larger doses it is a powerful hypnotic and in patients who have idiosyncrasy it may produce toxic symptoms In occasional cases it makes the patients peculiarly quarrelsome

A more recent introduction is primidone (Mysoline) which promises to be almost as useful an anti convulsant as phenobarbitone It is issued in tablets of 0 25 g of which from 1 to 6 may be taken in the day The toxicity of primidone is low and by itself it is not strongly hypnotic but if taken in association with phenobarbitone it may cause excessive drowsiness Another remedy is phenytoin sodium (Dilantin Epanutin Solantoin) which is usually dispensed in capsules of gr 1½ (0 1 g) For adults, 1 or 2 capsules may be given twice or thrice daily and smaller doses for children in proportion to size This drug has the merit of being less hypnotic than phenobarbitone but it is of less general usefulness and far more often produces toxic effects Of the latter, hypertrophy of the gums is the most characteristic but rashes and tremor also occur Phenytoin sodium has its most successful employ ment in cases in which nocturnal fits are numerous, two capsules being given (to an adult) at bedtime If it is decided to make a change to phenytoin sodium from some other medication this should be done gradually over several weeks

Recently the substance troxidone (Tridione) has been employed in the treatment of *petit mal* Given in doses of 0 3 g twice or thrice daily it has a striking effect in a minority of cases The occurrence of major attacks is a contraindication to its use and it is liable to give rise to toxic symptoms of which agranulocytosis is the most important It should therefore only be given under careful observation and when the treatment can be controlled by regular blood examinations

Many other remedies have been advocated in epilepsy a few only have stood the test of time and are still in use, both as alternatives and adjuvants to the treat ment above given These may be placed in order of merit as belladonna digitalis and borax

Whatever remedy is chosen it is essential if possible to anticipate the occurrence of the fit by the administration of the drug Thus if fits are nocturnal only the remedy is given in a single dose at night or if diurnal only, in a single dose in the early morning Again if as often happens the fits occur soon after waking then the single nightly dose should be used Or, if the fits occur or are more frequent at the menstrual epoch they should be anticipated by increased dosage before and during that epoch With fits that are diurnal and nocturnal a night and morning dose should be used Some patients do best on phenobarbitone alone others on another remedy alone and others on a combination of drugs and the best course can only be deter mined after trial

STATUS EPILEPTICUS —The treatment of this condition and that of rapidly re peated fits which not infrequently merges into status epilepticus is one of urgency and constitutes one of the important neurological emergencies

The first thing to be done is to check the convulsion and this is best achieved by inducing a state of light anæsthesia For this purpose paraldehyde in large doses is perhaps the safest and most effective drug If it can be administered by mouth ½ to 1 oz should be used in the case of an average adult or alternatively 1 to 2 oz may be given per rectum Subsequently smaller doses should be given every 2 to 3 hours in order to maintain a state of light narcosis the amounts being judged by the depth of unconsciousness and the occurrence of fits Alternatively amylobarbitone sodium (Sodium Amytal) gr 7½ given intravenously which is very effective may be employed If fits of great frequency and violence are present at the outset the situation can usually be temporarily controlled by the light administration of chloro form by inhalation Morphine gr $\frac{1}{6}$ with hyoscine gr $\frac{1}{100}$ may be of great value in controlling the restlessness of patients emerging from status but should be used with great caution owing to their depressant effect on the respiratory centre and

the danger of broncho pneumonia Together with the more immediately acting drugs phenobarbitone (gr 3) in the soluble form may be given intramuscularly and if necessary repeated in 12 hours Chloral and bromide are usually quite ineffective

An early opportunity should be taken to promote a vigorous action of the bowel either by the administration of a rapidly acting aperient such as castor oil by mouth or by an enema Care must be taken to protect the tongue from being bitten and to keep the mouth free from saliva and vomitus Tongue forceps should be at hand in case the tongue be swallowed during a period of coma and the patient should never be left alone As far as possible the chest should be supported on pillows between fits and the patient should be nursed on alternate sides Where persistent cyanosis is marked oxygen may be given together with 5 per cent carbon dioxide where hyperventilation is conspicuous Adequate fluid should be given preferably by mouth but when this is impossible by subcutaneous, intravenous or rectal drip of 5 per cent glucose in normal saline As consciousness returns a highly nutritious diet should be given in small frequent meals Hyperpyrexia may be controlled by frequent sponging or even by immersion in a tepid bath When consciousness returns the routine treatment of epilepsy should be resumed Status epilepticus carries a considerable mortality and death commonly occurs from broncho pneumonia or from cardiac failure Not infrequently status epilepticus is the terminal event in cases of chronic epilepsy

NARCOLEPSY

In this remarkable syndrome originally described by Gelineau and subsequently in greater detail by Adie and Wilson two quite different kinds of attack occur

The one is the onset of apparently normal sleep which comes on especially at time of inattention or when the desire to sleep might normally be expected to occur *as for example after meals in public vehicles or during the performance of tedious* duties The sleep is preceded by a sensation of extreme drowsiness often amounting to an irresistible desire to sleep The sleeper is easily roused and is then perfectly normal but if left undisturbed may remain asleep for many minutes or even an hour or two Attempts to ward off the attack by voluntary effort lead to an increase in intensity of the craving for sleep until it is satisfied

The other form of attack consists of a sudden onset of weakness and tonelessness in the voluntary muscles to which the term *cataplexy* is applied These cataplectic attacks are almost invariably precipitated by sudden emotion such as anger pleasure surprise or anticipation and most often of all by events provoking laughter In a severe attack when the emotion reaches a certain intensity the muscles suddenly become limp the head falls forward the jaw drops the eyelids close and the face becomes expressionless the arms fall to the sides and the legs crumple so that the patient sinks to the ground an inert mass speechless and incapable of the slightest movement but without any impairment of consciousness In a second or two the attack passes and the muscles immediately regain their normal condition Milder attacks may involve any part of the musculature or may consist merely of a momentary feeling of weakness of the knees Patients can often judge with great accuracy the intensity and nature of the emotion necessary to bring on an attack

Although most commonly the sleep attacks and cataplectic attacks occur under the characteristic circumstances in the same patients each may occur in isolation Often the patient complaining of one form of attack will admit to the other upon questioning though it may have been of rare occurrence and have caused little inconvenience

In the majority of patients suffering from narcolepsy examination reveals no evidence of organic disease in the nervous system or elsewhere and pathological

investigation is equally negative In such cases the term idiopathic narcolepsy can properly be applied Males are much more commonly affected than females, and though the attacks may begin at any age a large proportion have their onset between the ages of 10 and 30 and may continue throughout life In such cases it seems probable that we are dealing with a spasmodic disturbance of function of the nervous system comparable in many ways to epilepsy, though at present we have no clue to the cause of the disorder

In rare cases the narcoleptic syndrome may occur as a symptom of organic disease of the nervous system notably of encephalitis lethargica tumours of the third ventricle or hypothalamus and cerebral syphilis This association suggests that the site of the disturbance is in the autonomic centres of the hypothalamus and the floor of the third ventricle

Treatment —The sleep attacks of narcolepsy are in many cases greatly improved by the regular use of amphetamine sulphate An initial dose of 10 mg after break fast and lunch is often enough but this may be increased if necessary to 20 mg b d or even 30 mg b d Symptoms of overdosage are sleeplessness restlessness and tremulousness Less efficacious but of undoubted value in some cases is ephedrine sulphate in doses of gr ½ to 1 b d

Neither of these drugs is of comparable value in controlling the cataplectic attacks which usually remain resistant but can often be adequately prevented by the careful avoidance of the emotional stimulus which brings them on

MIGRAINE

Synonyms —Hemicrania Sick Headaches

Definition —A common malady of which the only essential characteristic is recurring intense headaches which usually develop on waking in the morning and which while often unilateral may be bi frontal occipital or general The attacks usually date from childhood but sometimes commence in later life The headaches are often associated with nausea and vomiting which has given rise to the designation sick headaches or bilious attacks and also with peculiar disturbances of vision and with giddiness suggestive of vestibular disturbance Less common symptoms of the disorder are varieties of slow sensory auræ which occur in no other malady attacks of hemiplegia or monoplegia or of aphasia and attacks of ophthalmoplegia Some of the phenomena may accompany the headaches but others occur in attacks quite apart from the headaches and may for that reason give rise to difficulty in diagnosis

Ætiology —The malady may originate in early childhood but commonly makes its appearance at about the age of puberty and tends to persist with fluctuations in the severity and frequency of attacks throughout adult and middle life It often ceases in women at the menopause and its persistence into old age in either sex is exceptional The sexes are equally affected and a history of family incidence is com mon In other cases a family history of such paroxysmal disorders as hay fever asthma urticaria or epilepsy or of psychopathic tendencies may be obtained Subjects of migraine are commonly of an energetic and intelligent type and many have a meticulous standard of thoroughness and precision almost amounting to an obsession

Nothing is known with certainty as to the essential cause of migraine Numerous factors such as errors of refraction disorders of digestion and of endocrine function and psychological disturbances have all been evoked as responsible causes but it is probable that at most they are never more than precipitating factors in susceptible individuals There is considerable indirect evidence that the immediate cause of the attack is a paroxysmal variation in the calibre of the cerebral blood vessels either

spasm or dilatation or the one followed by the other but proof is at present lacking

Precipitating factors are numerous and may be very specific. On the psychological level fatigue anxiety and frustration play an important part On the physical plane over exertion and fatigue indiscretions or irregularities of food exposure to excessive light or noise prolonged eye strain especially in the presence of an uncorrected error of refraction commonly figure in the history of migrainous subjects Women usually have attacks in association with the menstrual periods and often remain entirely free during pregnancy

Symptoms —The subjects of migraine are usually otherwise quite healthy and are often robust and strong Premonitory signs of the attacks are present in some cases and these may take the form of an unusual feeling of well being and intellectual acuity or on the other hand of lassitude and depression

The attack commences most commonly on waking in the morning when on raising his head from the pillow the patient experiences a sense of giddiness ocular confusion and nausea such as is commonly felt at the onset of sea sickness It is at this stage of the attack and within a few minutes of its commencement that the visual phenomena occur if these are present Often the patient vomits at once but some times vomiting is delayed for hours but may continue throughout the attack with great prostration sweating and coldness of the extremities The visual disturbances last but a short time (from 10 to 30 minutes) but leave as a rule some confusion of vision and discomfort throughout the attack The headache follows shortly after these initial symptoms It is cumulative and throbbing in character and often begins constantly in a localised spot over one eye or in the temple as a sharp boring pain which gradually spreads and may involve the neck and arm The pain may be unilateral frontal occipital or quite general but is usually constant from attack to attack As the headache increases in severity the face becomes pale and grey, the patient becomes much prostrated and is incapable of mental or physical effort and unable to take food Light noise and movement aggravate the pain intolerably and the patient seeks the refuge of his bed in a darkened room After remaining in this condition for some hours he falls into a deep sleep and wakes next day shaken by his illness but otherwise well

The above description covers many attacks of migraine but many variations occur The attacks do not always occur on waking they may come on at any time of the day or at night They may be rapidly transient lasting for a few hours only or they may last for days and give rise to much anxiety in the attempt to provide nourishment and sleep for the patient It is not uncommon for them to change their character gradually as the patient gets older and in cases of long standing the patient may complain of a persistent annoying headache between the attacks In other cases the headache may be relatively inconspicuous compared with the vomiting and the various sensory disturbance

Visual phenomena —Considering how very common migraine is it must be clearly understood that any visual phenomena except slight confusion of vision accompanying the attacks are rare They may take the form of general mistiness of vision floating spots scotomata bright stars and colours hemianopia double hemianopia with com plete blindness or psychic hallucinations of vision In connection with scotoma and with hemianopia the phenomenon of teichopsia may occur as follows Upon the dark background of the scotoma or hemianopic field a ball of light appears which grows larger and becomes dark in the centre This ring of light breaks at one spot opens out and takes the form of a series of entering and retreating angles (castellation figure) which become gloriously coloured (fortification spectrum) and which later become fragmented and fade These visual events usually occur at the very beginning of the attack before the headache develops and they are rapidly evanescent but they may occur as isolated phenomena when no headache occurs

Aphasic attacks may take the form of confusion of speech word blindness or even

loss of speech acceptance and exteriorisation They accompany the headaches and occur at the commencement of the attacks They are not of common occurrence

Sensory auræ —These are somewhat rare events but *they are pathognomonic of* migraine and may occur quite apart from the headaches The aura commences upon the periphery of a limb and is likened to that which would be produced by a multitude of cold footed insects creeping on the skin It travels very slowly proximally taking half an hour or more to reach from the fingers to the head and is very alarming to the patient It disappears rapidly without further event It is the only aura with an exceedingly slow spread Another form of sensory aura occasionally encountered is numbness of the lips and tongue

Ophthalmoplegia —This is a very rare but most important event It occurs only at the height of the headache, in severe attacks Indeed the patients usually say that the headache, during which the ophthalmoplegia occurred, was the very worst they had ever experienced It is a partial paralysis of the oculo motor nerve trunks most commonly of the sixth nerve alone but sometimes of the third or fourth nerves or of a combination of these three It is generally unilateral, but may occur simultaneously on both sides Severe diplopia results It passes off in from a few days to a few weeks When once it has occurred it is apt to recur with subsequent attacks Attacks of this kind have been called ophthalmoplegic migraine but it should be *realised that the ophthalmoplegia and the migraine syndrome are symptomatic of* some organic intracranial disease the nature of this cannot always be discovered by the means at present at our disposal but in many instances it is an aneurysm or angiomatous malformation which may be revealed by arteriography

Diagnosis —*In typical cases the diagnosis of migraine is seldom in doubt* The long history the familial incidence and the common association of headache with vomiting and various sensory disturbances all contribute to a characteristic clinical picture When however these varied manifestations occur alone considerable difficulty may be experienced

It is important to remember that tumours of the occipital lobes and intracranial aneurysms may be associated with attacks exactly resembling migraine and every case should be carefully examined for signs of organic nervous disease particularly papillœdema or persistent defects in the fields of vision It is probable that the so called ophthalmoplegic migraine in many cases at least is a symptom complex distinct from true migraine and dependent upon a gross intracranial lesion most often an aneurysm on one of the component vessels of the circle of Willis Hypertension with or without chronic renal disease, may be associated with headaches closely resembling migraine and an examination *of the blood pressure and of the* urine should never be omitted Headaches of neurotic origin may closely simulate migraine particularly when as is not infrequently the case they are superimposed upon a background of true migraine It is exceedingly rare for migraine to recur *more often than once in 2 or 3 weeks* or to last more than 2 days in persons without a strong neurotic tendency

Those who are not familiar with the full range of sensory symptoms that may precede the onset of the headache and do not realise the severity of the speech disturbances which in some cases accompany them are apt to take an unduly grave and erroneous view of the history given by a patient who has experienced them Thus a diagnosis of epilepsy or of cerebral tumour is not infrequently made It should therefore be remembered that the disturbances of sensation which occur in epileptic attacks are momentary in duration and never persist as do the migrainous symptoms in question for many minutes *Again consciousness is neither* blunted nor lost in migraine

Attacks of migraine consisting wholly of vomiting and sometimes associated with diarrhœa and abdominal discomfort are readily mistaken for abdominal disorders

Treatment —Few non fatal disorders are more stubbornly resistant to treatment

than migraine Many victims suffer from recurring attacks throughout the most valuable years of their lives to the serious detriment of their work and happiness In many cases help can be given by attention to general health and physical and mental well being for a lowering of these in a migrainous subject seldom fails to evoke an increase in the number and severity of attacks In others it may be possible to eliminate precipitating factors whether physical or psychological in nature but only too often when these are discoverable they are found to be amongst the unalterable features of the patient s environment

Drugs administered consistently over a long period may be of value in some cases and of these phenobarbitone gr ½ twice daily or gr 1 at night is perhaps the most generally useful Gowers mixture containing min 1 of liq trinitrini min 5 of liq strychninæ min 10 of tinct gelsemii and gr 10 of sodium bromide administered thrice daily has long enjoyed a favourable reputation largely from lack of competition The individual attacks are equally difficult to relieve Sometimes a full dose of phenazone acetanilide phenacetin or aspirin given at the very commencement of an attack will ward it off but are useless when once the headache is fully developed Ergotamine tartrate (Femergin) in doses of ½ to 1 mg by mouth or injection will sometimes cut short an attack but is by no means the specific that has been claimed When attacks are frequent one or two tablets of ergotamine tartrate daily may be used as a prophylactic Apart from these remedies it remains to keep the patient as comfortable as possible and to induce sleep by the use of ordinary hypnotics and to secure that the patient takes adequate fluids and nourishment during a prolonged attack

DISORDERS CHARACTERISED BY INVOLUNTARY MOVEMENTS

WILSON S DISEASE *(see p 1484)*

PARALYSIS AGITANS

Synonyms —Parkinson s Disease The Shaking Palsy

Definition —A progressive disease of insidious onset and slow course usually occurring in the second half of life and characterised by loss of the normal associated movements and by a peculiar stiffness of the muscles which give rise to a distinctive facial expression bodily attitude and gait The stiffness is accompanied by weakness and often by rhythmic tremors which have earned for this malady the name shaking palsy

Ætiology —Little is known of the causal factors of this malady It is essentially a disease of the decline of life and though in rare instances it is met with as early as the eighteenth year *the maximum incidence is from the fiftieth to the seventieth* year Men suffer twice as frequently as women Heredity seems to play no part in the causation

Pathology —No naked eye changes are to be found other than associated vascular and degenerative changes which are common in senile conditions The most definite pathological findings are degenerative changes in the cells and fibres of the corpus striatum and its efferent systems These changes are most marked in the globus pallidus of the lenticular nucleus but occur also in the putamen the caudate nucleus the corpus Luysii and the substantia nigra There is a constant loss of cells preceded by degenerative changes in those that remain An associated glial proliferation takes place in the affected regions together with fibrosis in the smallest arterioles and capillaries The relationship of these changes to the symptomatology of the disorder

loss of speech acceptance and exteriorisation They accompany the headaches and occur at the commencement of the attacks They are not of common occurrence

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Treatment —Few non fatal disorders are more stubbornly resistant to treatment

acteristic feature of the tremor in about one half of the cases is that it continues during repose and is temporarily arrested by the execution of volitional movement In the other half of the cases however the tremor appears or is increased on voluntary exertion and tends to be less during repose There seems to be an antagonism between the tremor and the rigidity for in cases where the rigidity is very conspicuous the tremor is little marked or absent and conversely when tremor is universal or is of early onset rigidity is a less noticeable feature

Other symptoms of the disease which are very commonly complained of are—(1) difficulty in turning over in bed which is the obvious result of the rigidity of the trunk muscles (2) flexion of the toes into the sole of the foot so that they are trodden on from spasm of the plantar muscles (3) pain of a dull aching character in the trunk and limbs which is presumably produced by the long continued traction of the rigid muscles upon their attachments (4) abnormal sensations of heat and cold and (5) hypersensitiveness to changes of temperature—the patient cannot bear to be near a fire nor yet in a cold room Mental symptoms are conspicuous by their absence except in the last stages of the malady when profound asthenia overtakes both mind and body The constant bodily discomfort, restlessness sensations of fatigue which the rigidity and the tremors engender and the consciousness of a malady which is found only too soon to resist every effort to lessen or arrest it often result in gloomy and lasting mental depression Objective sensibility is unimpaired The special senses and the cranial nerves are not affected The sphincters and the reflexes are normal Trophic changes in the periphery of the limbs thinning and glossiness of the skin with fluted nails and vasomotor disturbance are common Bed sore is commonly met with in the late stages of the malady

Diagnosis —There are three points which can be surely relied upon to render the diagnosis of paralysis agitans certain in every case namely—(1) the aspect of the patient when he is walking when the fixed mournful expression the stooping attitude with round shoulders the elbows pressed into the side and the hands carried across the abdomen in the interosseal position the immobility of the head and neck and the curious gliding gait which cannot fail immediately to arrest the observer s attention (2) the rhythmic rolling tremor which is quite unlike any other form of tremor and which often continues during rest and (3) the absence of any of the signs of disease of the pyramidal system Difficulty may perhaps be experienced when the aspect is little marked and the tremor is confined to some unusual situation such as the face tongue or neck but if the possibility of tremor in any situation being that of paralysis agitans be borne in mind its rhythmic rolling nature will give the diagnosis When paralysis agitans is confined to one side of the body the appearance of the patient may superficially resemble that of hemiplegia but in these cases the peculiar aspect of paralysis agitans is marked and the organic signs of hemiplegia such as the extensor response in the plantar reflex the increase in the deep reflexes and the absence of the abdominal reflex upon the paretic side are not present In senile tremor the rhythmic rolling quality is absent and the aspect is not that of paralysis agitans In post hemiplegic tremor the organic signs of hemiplegia are present Toxic tremor is irregular and never rhythmical and is (mercurial tremor excepted) a fine tremor The intention tremor of disseminated sclerosis cerebellar disease and lesions of the red nucleus are so peculiar and so widely different from the tremor of paralysis agitans as to render confusion impossible

The one clinical condition which may resemble paralysis agitans so closely as to be indistinguishable is the form of Parkinsonism which may appear as a sequela of encephalitis lethargica In this condition there are similarly placed changes in the basal ganglia brought about by the encephalitic virus Such post encephalitic cases commonly originate much earlier in life than paralysis agitans and there may be a history of the initial disease The onset is often more rapid and the condition may become arrested whereas paralysis agitans is invariably relentlessly progressive

is by no means clear the more so in view of the fact that in the post encephalitic cases the principal changes are found in the substantia nigra

Symptoms—The onset is always insidious and the paucity of movement and the muscular rigidity are almost always the first signs to appear This *rigidity* affects the face neck and trunk to a greater extent than the limbs and when the limbs are affected then the proximal muscles present a greater degree of rigidity than do those of the periphery The oncoming rigidity of the facial muscles does away with the usual play of the emotional movements in facial expression and the face assumes a fixed anxious and mask like expression, with absence of the usual involuntary nictitation The voice loses its inflexions and becomes monotonous from rigidity of the muscles of larynx tongue and lips, but there is no other defect of articulation Very striking is the effect of the rigidity of the muscles of the neck for the patient carries his head and neck in one piece with his trunk as if he were a statue, never inclining or raising it in the customary expressive manner and if he turns round to look at anything he tends to move the whole trunk round with the head In looking sharply to one side the eyes move before the head whereas under normal circumstances the coarse adjustment of this movement is done first by the neck muscles and the fine adjustment subsequently by the eye muscles The stiffness of the trunk muscles gives a stooping attitude with the head inclined forwards while that of the upper extremities causes the shoulders to be rounded and the arms carried with the elbow semiflexed and pressed into the sides The gait is highly characteristic in marked cases since on account of rigidity of muscles it is deprived of spring and suppleness the patient in the characteristic attitude above described takes small gliding steps displacing his centre of gravity as little as possible If by any circumstance such as catching the feet against an unevenness of the ground or a push the centre of gravity is much displaced the patient often has a difficulty in regaining it and in moving to recover his centre of gravity is unable quite to catch it up and so continues the movement of necessity until he fall or come in contact with some object by which he can arrest himself and restore his balance This phenomenon is more often seen in advanced cases and is known as propulsion retropulsion and lateripulsion according as the centre of gravity is displaced and the movement occurs in a forward backward or sideways direction Festination is the term used for the quickening of the pace sometimes seen in this attempt to overtake the displaced centre of gravity In the hand the rigidity is greater in the interosseal muscles and the hand therefore tends to assume the interosseal position with the fingers pressed together and the *thumb adducted the metacarpophalangeal joints being flexed and the interphalangeal* joints extended From this rigidity of the hand the writing becomes small as well as tremulous and the patient finds it difficult to write in a straight line Muscular weakness always accompanies the rigidity and the tremors It is slight until the late stages of the disease when it may increase rapidly and render all useful movement impossible On account of the rigidity and consequent slowness of movement the patient experiences a sense of weakness which is much greater than the actual weakness shown by the dynamometer *Tremor* is present in the majority of cases It usually commences in the hand and forearm and is most conspicuous in this situation but it may be seen in the face tongue jaw neck and feet while in rare cases it may be universal The nature of the tremor is peculiar and is highly characteristic It is a regular rhythmical contraction of the muscles alternating in the opposing groups with a frequency of from four to six oscillations per second with a range of from an eighth to three quarters of an inch Its rhythmic nature its slowness and its range distinguish it from other varieties of tremor In the hand the characteristic movement of the tremor is the rolling together of the opposed thumb and fingers cigarette rolling bread crumbling or drum tapping movement. There is nearly always in addition a peculiar pronator supinator tremor The tremor is increased by excitement and by self consciousness and ceases during sleep A highly char

acteristic feature of the tremor in about one half of the cases is that it continues during repose, and is temporarily arrested by the execution of volitional movement In the other half of the cases however the tremor appears or is increased on voluntary exertion and tends to be less during repose There seems to be an antagonism between the tremor and the rigidity for in cases where the rigidity is very conspicuous the tremor is little marked or absent and conversely, when tremor is universal or is of early onset rigidity is a less noticeable feature

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Post encephalitic cases often manifest other sequelæ of the disease, notably oculogyric crises post encephalitic tics alteration in the pupils or external ocular muscles and changes in temperament These are absent in paralysis agitans

Course and Prognosis—Paralysis agitans often begins in one limb usually the upper, and spreads thence to the corresponding limb of the opposite or to the other limb of the same side In the latter case it has approximately a hemiplegic distribution and it may remain for years much more evident upon one side of the body The course is *slowly progressive with variable rate* In some cases the malady may remain stationary for years, and this is more often seen in middle aged subjects, before the disease has reached an incapacitating stage Such arrest in the early stages is not often seen in young subjects for in the latter the disease seems to take a more continuously downhill course Real improvement in the symptoms is never seen A fatal issue may occur in as short a time as 2 years, but this is exceptional, since paralysis agitans has little tendency to shorten life The average duration is from 10 to 15 years and *since the major incidence of the disease is in the sixth decade of life it will be seen* that many of the patients are of average longevity Death may occur from intercurrent maladies especially from bronchitis but more commonly after the lapse of many years the patient becomes bedridden from increasing weakness and rigidity and sinks into a condition of sleepy asthenia which is soon terminated by coma An unduly high blood pressure is unusual in the subjects of paralysis agitans and it is noteworthy that they do not suffer from gross cerebral vascular lesions such as thrombosis or hæmorrhage

Treatment—All that can be done to arrest or slow down the degenerative process which is responsible for the symptoms is general tonic treatment and the administration of those vitamin B elements which aid the general nourishment of the nervous system Palliative treatment is almost entirely medicinal Where there is much rigidity gentle exercise, passive movements and massage are useful *but electrical* treatment can do no good In using the various medicinal remedies which are available, it must be remembered first that all of them produce their effect for a few hours only and secondly that the patient s symptoms cease in any case during sleep It is therefore important that the patient should take the drugs at such times of the day as to obtain the maximum relief during those periods when he most desires it *and* it is useless to take them at night The most generally useful remedy is benzhexol hydrochloride (Artane) *which relieves* both the tremor and the rigidity though in occasional cases by reducing the rigidity it allows the tremor to increase It is issued in tablets each containing 2 mg or 5 mg and small doses should be given *until* the patient s tolerance of the drug is assured it can then be increased *gradually up* to 20 or 30 mg in the day until the maximum effect is obtained The symptoms of *intolerance are nausea and occasionally some blurring of vision*

The action of procyclidine hydrochloride (Kemadrin) is similar Drugs of the belladonna group have long been used—belladonna hyoscine stramonium atropine and of these hyoscine is in general the most valuable It may be given in tablets (each gr $\frac{1}{200}$) or in solution and the latter has the advantage that the dose is more easily varied (gr $\frac{1}{200}$ or $\frac{1}{100}$ *by mouth thrice daily in chloroform water*) If quickly absorbed it may produce feelings of confusion or faintness and should therefore not be taken when the stomach is empty but only after food The combination Rabellon contains hyoscine stramonium and atropine in tablet form

The progress of the disease is slow and the patient should be encouraged to maintain his *activities as long as possible nothing* is to be gained by rest When the patient is bedridden great care must be taken with the skin

Pains may be troublesome and can only be relieved with aspirin and similar analgesics The immobility of the limbs may cause arthritis in the *shoulders and* this should be guarded against by passive movements and when it occurs treated by the usual appropriate *measures*

CHOREA

Synonyms —St Vitus Dance Sydenham s Chorea Rheumatic Chorea

Definition —Chorea is an affection of the nervous system characterised by the occurrence of spontaneous involuntary movements, irregular both in time in extent and in place of occurrence and also by muscular weakness and by a variable degree of psychic disturbance

Ætiology —The important causal factor of the ordinary variety of chorea is acute or subacute rheumatism Chorea is much more common among the poorer classes than among the well to do Its incidence is upon nervous highly strung subjects rather than upon the phlegmatic and this is probably to be explained by the fact that the rheumatic subject is likely to be nervous and highly strung Chorea is practically unknown during the first 3 years of life and is very rare before the fifth year has passed Common between the ages of 5 to 10 years it reaches its maximum incidence between 10 and 15 years After the age of 20 it is rare except in pregnancy but a few cases have been reported up to the age of 60 years which have certainly been examples of rheumatic chorea Females are affected twice as frequently as are males Heredity concerns the incidence of chorea in two ways firstly in the inheritance of the rheumatic tendency which is the important cause of chorea and secondly in the inheritance of the neuropathic tendency for it is when these two are coincident that chorea is most prone to occur As early as 1802 rheumatism was regarded as the cause of chorea and all subsequent investigations have upheld this theory The family history of a choreic patient generally brings to light the occurrence of acute rheumatism of cardiac disease and of other rheumatic manifestations among other members of the family Often the patient has suffered with acute or subacute rheumatism growing pains rheumatic erythema purpura rheumatic nodules or recurrent sore throat before the appearance of the chorea and may be found to be already the subject of rheumatic heart disease A large percentage of those patients who have never shown any sign of the rheumatic state before or during the attack of chorea subsequently suffer with rheumatic symptoms The British Medical Association Collective Investigation Committee found that rheumatism preceded the chorea in 26 per cent of the cases and that in 46 per cent of the remainder rheumatic signs accompanied the chorea or appeared subsequently If to the total of choreic patients who present rheumatic signs at some time or other one adds those with no personal history of rheumatism but with a family history of rheumatism it will be found that there are but few cases of chorea in which a personal or family history of rheumatism is absent

Psychical disturbances —Any emotional disturbance such as fright anxiety depression or overpressure in school may sometimes act as an immediate determining factor but much more often these events simply aggravate symptoms which are already present in slight degree

Pregnancy —The relationship of pregnancy to chorea is very definite It is generally met with in first pregnancies and before the age of 25 years and in most cases the pregnancy appears to be the only immediate cause for the chorea but a history of rheumatic infection will often be obtained in a careful history The onset of the chorea is usually between the first and third months of pregnancy It is liable to recur with subsequent pregnancies

Pathology —The essential lesion has proved very difficult of detection by microscopical investigation but according to Greenfield and Wolfsohn it consists in a diffuse meningo encephalitis affecting mainly the basal ganglia the cerebral cortex and the pia arachnoid

Symptoms —The onset is usually gradual but it is sometimes abrupt when emotional disturbance has been the determining cause The appearance of choreic

movements is often preceded by alterations in the mental and physical condition of the child She becomes nervous and more impressionable than before She is increasingly unable to apply her attention She becomes clumsy in her movements—and lets fall objects which she is holding Anæmia apathy and languor and irregularity of appetite are commonly present At this time, careful observation will discover slight involuntary movements of the face and fingers which are often unilateral in distribution From day to day the movements become more marked and spread *to the limbs and trunk* *The face is constantly grimacing* and the hands and arms scarcely cease from turning about and affection of the legs makes the walking irregular and clumsy The child can no longer keep still the respiratory movements become irregular and spasmodic and the chorea is fully developed The characteristic symptoms of a well marked case of chorea are—(1) involuntary movements (2) *weakness of voluntary movements* (3) *ataxy or loss of precision of voluntary movement*, (4) emotional instability and other psychic disturbances

1 THE INVOLUNTARY MOVEMENTS are always irregular in time and in the form of the movement Similar movements are never repeated successively in the same part. Each movement begins rapidly and ends suddenly, and one frequently sees the involuntary movement complicated by the addition of a voluntary movement to cover the fault The majority of the movements are complicated involving several muscles and often more than one joint In the face the more simple movements take the form of asymmetrical twitches in the lips and about the angles of the mouth and orbits In more severe cases the strangest grimaces may occur The tongue is thrust into one cheek then put out and withdrawn just in time to escape the sudden snap of the open mouth When asked to show the tongue the child puts it out rapidly and holds it there by closing the teeth upon it Smacking of the tongue and palate may often be heard at a distance Lateral movement of the jaw is common According to the severity of the case speech may be difficult the words being articulated slowly in slurred monosyllables For the same reason swallowing may be difficult or impossible in severe cases and may necessitate nasal feeding The ocular muscles participate in the involuntary movements only in very severe cases

In the upper extremities the movements appear first in the hand The thumb is more restless than the fingers which are spread and pressed together flexed and extended alternately the wrists twist about irregularly the forearms are constantly agitated with movements of *pronation and supination flexion and extension* while all possible movements of the shoulder occur When the upper extremities are outstretched the hands assume the position of flexion at the wrist and over extension at all the finger joints in so many of the cases as to make this a characteristic feature of chorea The lower extremities are less severely affected than is the rest of the body and here the movements are best seen when the child is lying down The gait tends to be clumsy and insecure and in severe cases walking becomes impossible Alteration of the rhythm of the respiratory movements is conspicuous and is highly characteristic of chorea The breath is often taken rapidly and held for some time then let go with a loud sigh The trunk is often involved and movements of a writhing nature are characteristic

So far as the limbs are concerned the movements may be confined to *one side* more commonly the left side and the condition is then called hemichorea but the involvement of the face and trunk is always bilateral and is generally equal upon the two sides In hemichorea the movements are always of slight severity Severe chorea is never confined to one side Choreic movements cease during sleep and except *in severe cases* *can be controlled more* or less by voluntary effort the attempt to write for example will generally cause cessation of the movements of the right arm for the time being They are generally increased by observation emotion and self consciousness but in a few cases it will be found they are worse when the child is alone and unobserved The violence of the movements *of the limbs* may cause the

skin over the prominences to ulcerate from friction against their clothing and the head and limbs may be badly bruised from contact with adjacent objects and unless the patient be properly protected wounds may occur, which are liable to infection

2 LOSS OF POWER is shown in the mild cases by incapacity for exertion and undue fatigue More severe degrees of paresis may accompany or succeed the appearance of the movements It may be observed that in one limb, or upon one side of the body the choreic movements are becoming less marked, and that the limbs are becoming progressively weaker Soon the arm hangs loosely by the side and the leg is dragged in walking The degree of choreic paralysis bears no relation to the severity of the movements for the former may be severe, when the latter are slight and vice versa Choreic paresis is apt to return with successive attacks of chorea but not always in the same region

Limp chorea (*chorea mollis*)—This is a more severe degree of choreic paralysis which may affect the whole musculature but is more often of hemiplegic distribution It may be preceded by the usual symptoms of chorea More often the paralysis is the first noticeable symptom and this develops rapidly in from 24 to 48 hours The paralysis is characterised by complete flaccidity of the limbs, the child lies upon its back and does not move and if one of the limbs be raised from the bed and then released it falls limp and lifeless The head is no longer held in a natural position but falls round on to the ear Careful investigation however, rarely fails to reveal some slight choreic movements either in the face or in the fingers Paretic chorea and chorea mollis run a benign course and recovery is said to be almost invariable

3 INCO ORDINATION OF VOLUNTARY MOVEMENT may be the first symptom of chorea to attract attention and it may precede the appearance of the choreic move ments It may be very obvious when the movements are slight and it is mo t noticeable in those of the hand and forearm which lack precision and in those of articulation deglutition and respiration The involuntary movements that have been described are superimposed upon voluntary movements which they render inco ordinate at times interrupting them abruptly and at other times tending to prolong them

4 PSYCHICAL DISTURBANCES are common some degree of emotional instability failure of attention and depression being present in most cases and, generally in proportion to the severity of the affection The patient s behaviour changes she may laugh or weep without sufficient reason she may become capricious irritable and obstinate attention and memory are usually impaired and less interest is taken in the surroundings A condition of hebetude may develop Delirium may occur in acute and grave cases It is usually violent and loquacious and resembles other forms of toxic delirium and it is of serious prognostic import Visual hallucinations of a terrifying character may occur Mania is quite exceptional in children but it is not an uncommon complication in adolescents and adults The psychical disorders slight or severe usually disappear with the chorea and in all cases the prognosis as regards permanent mental recovery is good

The pupils are frequently dilated and may be unequal and eccentric and hippus may be present Sensibility is not impaired The sphincters are not affected The skin reflexes are normal The deep reflexes are also normal in a large proportion of cases but often the knee jerk shows an alteration which is peculiar to chorea On tapping the patellar tendon the resulting contraction of the quadriceps is unduly sustained and the leg remains in a position of extension at the top of its excursion for several tenths of a second in other cases a pendular knee jerk is present In severe cases the deep reflexes may be diminished and rarely may be absent for months

RHEUMATIC MANIFESTATIONS —Cardio vascular changes are common in chorea In nearly all the cases careful and repeated examination of the heart will reveal slight dilatation and reduplication of the second sound often with reduplication of the first sound and increased rapidity of the pulse Doubtless these are signs of

myocardial involvement resulting from the rheumatic infection Irregularity of the pulse may be dependent upon the altered rhythm of respiration Systolic murmurs are common and these may be hæmic in nature or may be the expression of cardiac dilatation but in the majority of cases they are indicative of endocarditis Endocarditis is present in 90 per cent of the fatal cases At least one half of all cases present cardiac murmurs which are suggestive of the presence of endocarditis while *some cases with no cardiac murmur during life are found post mortem to have endocarditis* The mitral valve is commonly affected lesions of the aortic valve being uncommon Pericarditis is a frequent associate of endocarditis, only in rare instances does it occur alone The valvular affections which are met with in chorea may be the result of antecedent rheumatism, or they may develop in the course of the chorea, or while no signs of endocarditis are present during the attack the patient may shortly afterwards present the signs of organic valvular disease Cutaneous affections which occur in rheumatism are met with also in chorea namely erythema purpura and subcutaneous nodules Acute articular rheumatism is comparatively rare and when it occurs it is usually accompanied by a cessation of the choreic movements When rheumatic phenomena are present and in the acute mania of chorea pyrexia is usually present but uncomplicated chorea is an apyrexial disease

RECURRENCE —One third of the subjects of chorea have more than one attack. Females are more prone to a recurrence than males in about the same proportion as they are more liable to original attacks The average interval between the attacks is 1 year If therefore a patient has remained well for 2 years it is improbable that a recurrence will take place The greater the number of choreic attacks, the more likely is the heart to be found affected and therefore cardiac complications are more often met with in recurrences In a recurrence of chorea the symptoms are usually less severe and their duration shorter than in the original attack

Course and Prognosis —The disease tends to a spontaneous termination after a variable time which is usually from 6 weeks to 6 months The duration rarely *falls short of the earlier period The average duration of cases treated in hospital* has been found to be 10 weeks Cases which last for more than 12 months are not rare and slight cases with remissions may last several years The course of the malady is that after a gradual development of symptoms there is a stationary period during which symptoms are well marked followed by a period of gradual diminution In some of the more severe cases of chorea where deglutition is difficult the patient is likely to be insufficiently fed and this constitutes a grave danger since in the condition of semi starvation so induced the chorea develops apace In such cases articulation and swallowing become impossible and the movements become ceaseless so that both rest and sleep become gravely impaired the patient wastes rapidly and is in danger of death from exhaustion unless prompt measures for restoring the depleted nutrition are taken This is the condition known as chorea gravis

The proportion of fatal cases occurring in chorea is less than 2 per cent Death is most often met with in first attacks occurring about the age of puberty and in cases associated with pregnancy It is very uncommon in young children and in recurrences of chorea

Diagnosis —The nature of the involuntary movements of chorea is usually so characteristic as to make diagnosis easy and to avoid any confusion with other maladies which present conspicuous involuntary movements *Nevertheless occasionally* a case of multiple tics in a child does present difficulties for the movements are not—as is so commonly stated—invariably repetitive In chorea the involuntary movements may lead to the dropping of objects from the hands This does not happen in the case of tics Again when the *choreic subject* gives the observer a firm and sustained handclasp, the irregular waxing and *waning* of the muscular contraction may be felt throughout by the observer In a case of *tics* the contraction is steadily maintained as in the normal subject In myoclonus the movements are short and

shock like while in athetosis they are slow and writhing In chorea mollis or hemiplegic chorea the paresis is in itself highly characteristic It is a flaccid paralysis which is never absolute and usually affects the arm most. There is no pain and no wasting and while spasticity is absent the deep reflexes are usually preserved

Treatment —It is well to commence treatment in every case with several days absolute rest in bed but in the milder cases this need not be persisted in beyond a few days though the ordinary periods of rest should be prolonged

The salicylates are of great value and of these aspirin is the most useful and it is best combined with equal doses of sodium bromide gr 10 of each may be given in mixture thrice daily after meals for a child between the ages of 8 and 14 and aspirin should be continued well into convalescence

In addition tonics such as syr ferri phos co (Parrish) and cod liver oil and malt are valuable especially in the convalescent stage

Severe cases of chorea call for skilled nursing The sides of the cot or bed should be well protected by pillows and the patient s hands and elbows covered with pads of cotton wool An unbreakable feeding cup is necessary When swallowing is difficult resort should be made to nasal feeding especially because of the importance of ample nourishment in this disease In the worst cases morphine may be required at night

HUNTINGTON S CHOREA

Synonym —Hereditary Chorea of Adults

This is a somewhat rare disease in which symptoms almost identical with those of rheumatic chorea namely involuntary spontaneous movements ataxy paresis and slow and slurring articulation gradually appear in adult life and usually about the age of 40 years and are accompanied by progressive mental failure with delusions and suicidal tendency The choreic movements are seldom severe but the inco ordination may be well marked Maniacal outbursts are not uncommon The disease always progresses slowly to a fatal termination in from 5 to 30 years and treatment is entirely unavailing It is a familial disease and the transmission is direct from parent to child but if a generation escape the malady it seems not to reappear subsequently Sporadic cases in which no heredity can be traced do however occur The sexes are equally affected Further than the heredity no causal factors are known The morbid anatomy consists in a slow progressive degeneration of the nerve cells of the basal ganglia and of the cerebral cortex with consecutive atrophy of the convolutions neuroglial overgrowth and meningeal thickening

APOPLECTIFORM CHOREA

This title has been given to rare cases of chorea of sudden onset in elderly subjects The involuntary movements are usually unilateral and are often of great severity and large amplitude (hemiballismus)

In cases of this disorder examined after death thrombotic softening or hæmorrhage has been found in the subthalamic region particularly in the corpus Luysii The mechanism by which small lesions in this situation give rise to such violent manifesta tions is not understood but the occurrence of such cases is obviously of great theoretical importance

SENILE CHOREA

A malady in which typical choreic movements constitute the chief feature is met with in elderly people and is possibly due to a progressive neuronic degeneration in those regions affected in the other forms of chorea It differs from Huntington s chorea in the late onset the absence of heredity and in the absence of mental changes

MYOCLONUS

Synonym —Paramyoclonus Multiplex (Friedreich) Myoclonus Epilepsy (Unverricht)

The characteristic symptom of this very rare condition is the occurrence of sudden shock like contractions of the muscles which may vary in intensity from simple fibrillary twitching to contraction which causes a violent movement of a limb The movements are often symmetrical, and are especially incident in the proximal muscles of the limbs

Ætiology —The malady appears in children usually between the ages of 5 and 15 years while in adults it commences between the ages of 25 and 40 years Both sexes are liable to the affection Many instances in which several children of the same parents have been affected have been recorded and in a few the malady has been transmitted through several generations There is now good pathological evidence that in some cases the condition is associated with diffuse cerebral lipoidosis and is related on the one hand to subacute inclusion body encephalitis and on the other to the various forms of cerebro macular degeneration while in other cases the peculiar bodies described by Lafora are found in the cells of the brain and also in the liver heart and possibly other organs

Symptoms —The movements of myoclonus are simple sudden movements and may exactly resemble the movement resulting from a single faradic stimulus Each movement commonly involves a single muscle only and it may concern no more than a few fibres resembling then the fibrillary twitching common in progressive muscular atrophy In other cases many muscles may be implicated in the shock like spasms which may be of so violent a nature as to throw the patient to the ground The distribution of the contraction is never determined by that of the nerve supply nor do the muscles contract according to their synergic association Myoclonic movements are irregular as regards rhythm and range of successive movements The upper limbs are more affected than the lower, and the proximal parts more than the distal while the periphery the hand and foot often escape Voluntary muscular effort usually checks the myoclonic movements but in rare instances it excites or augments the spasm The electrical excitability of the muscles is unaltered and there is no muscular wasting but the mechanical excitability of the muscles is increased and percussion of a muscle may evoke the spasms The sphincters are unaffected The reflexes both superficial and deep are normal Sensory phenomena are absent Speech may be seriously interfered with when the muscles of jaw tongue palate and larynx are implicated and spontaneous laryngeal and pharyngeal noises may occur The ocular muscles seem never to be the seat of the movements Epileptiform convulsions are present in the typical cases

Characteristic electro encephalographic changes have been recorded

Diagnosis —This is not difficult since the simple shock like movements in symmetrical muscles without any resemblance to volitional movements and entirely destitute of rhythm occur in this disease alone

Course, Duration and Prognosis —Myoclonus as a rule is a slowly progressive affection up to a certain stage and when this is reached it may remain stationary for years having little tendency to shorten life death ultimately occurring from some other disease without any period of freedom from the spasms Rarely the disease has ended fatally within a few months of the onset with progressive mental failure and coma

Recovery may take place spontaneously but the affection is very prone to recur

Treatment —Every available measure should be used to improve the general bodily condition so as to bring about a more stable condition of the nervous elements by improving their nutrition Sedatives may be tried but are seldom of value Myanesin taken by mouth relieves or abolishes the twitchings temporarily

SPASMODIC TORTICOLLIS

Definition —A disease of the nervous system characterised by tonic and clonic contraction of the superficial and deep muscles of the neck causing the head to assume either a position in which it is turned to one side and upwards or a position of marked retraction (retrocollic spasm) It is more correctly to be regarded as a disturbance of movements than of muscles and perhaps physiologically considered it may be spoken of as a disorder in the carriage of the head This carriage is a more complex and highly co ordinated function in the erect posture than in the quadru pedal posture it is a function peculiar to man and in this sense is of recent evolu tionary development. We may perhaps see in this a factor determining its frequent derangement as in spasmodic torticollis

Ætiology —The disease is most frequently met with in middle aged or elderly subjects but it may occur at any age from puberty onwards It is twice as frequent in females as in males The causation is most obscure Not infrequently neuropathic heredity such as epilepsy and insanity exists and the patients are often of highly strung nervous irritable dispositions Nervous shock prolonged anxiety and general ill health have frequently preceded the onset of symptoms Less often local strain or injury and exposure to cold have been the presumably exciting causes In a few cases it appears to develop from an occupation neurosis it developed for instance in a tailor who in drawing each stitch had the habit of making a short jerking move ment of the head to one side It occasionally occurs as a symptom of hysteria but such cases should be carefully separated from those in which there is no hysterical manifestation as being more susceptible to treatment and having less tendency to recur when once cured A torticollic movement may occur as a variety of tic. Typical torticollis may occur as the end result of lethargic encephalitis

Pathology —No morbid anatomical changes have been found On account of the involvement of several muscles, effecting special movements in this disease (as is well instanced by the over action of the frontalis in retrocollic spasm for retraction of the head is always normally associated with raising of the eyebrows in the act of looking up) it is probable that torticollis is due to disorder of those centres which direct such associated movements of the affected muscles

Symptoms —The onset is usually insidious but in rare cases may be quite sudden as in the case of a man aged 40 years who when walking along a London street suddenly turned his head at the sound of an accident which shocked him severely he was unable to turn his head back without using his hands to do so and he subsequently developed the most severe torticollis The initial symptom is always spasm which may be either tonic or clonic and frequently both forms of spasm are combined in the same case In the tonic form the head is retracted and the face turned to one side usually the left and owing to the retraction of the head the face is turned upwards The shoulder on the side to which the head is inclined is usually raised In severe cases all the muscles of the upper extremity the scaleni and the face muscles may become involved The spasm except in the earliest stages always involves muscles of both sides of the neck Where the bilateral involvement is general and equal the rotation of the head does not recur but it becomes strongly retracted and the condition is then known as retrocollic spasm Such retrocollic spasm is always accompanied by marked over action of the frontales the skin of the forehead being thrown into transverse wrinkles In the clonic variety there is jerking movement of the same muscles usually associated with some degree of tonic spasm The eyes do not follow the movements of the head in the jerkings The muscle primarily involved is the sterno mastoid the action of which is to incline the head forwards and towards the shoulder of the same side and rotate the face to the opposite side The next muscle involved is the splenius of the opposite side, which inclines

the head backwards and rotates the face towards its own side its rotatory action thus coinciding with that of the opposite sterno mastoid When the splenii of both sides act together the head is strongly retracted Next to be affected are the upper parts of the trapezii and the deep neck muscles and with further spread of the spasm any neighbouring muscles of the shoulder and upper extremity may be affected Sleep causes cessation of the clonic spasm but not always of the tonic spasm when the case is severe The spasm is always increased by fatigue and excitement. There is no wasting of the muscles involved but on the other hand they may be even hypertrophied if the spasm has existed for long and their electrical excitability may be increased The amount of pain associated with the spasm varies greatly There may be a slight feeling of cramp only but usually there is a great deal of aching pain, which may radiate down the arm and into the side of the head and make life unbearable to the patient More rarely sharp neuralgic pains are present

The course of the disease which has no tendency to shorten life is chronic exacerbations and remissions under treatment being common and recurrence, after temporary cure, frequent

Diagnosis —This is usually quite simple Fixed positions of the head associated with spasm occur in disease of the cervical spine, especially in spinal caries and are also associated with enlarged lymphatic glands in the neck The local signs of these conditions however are characteristic

Treatment —Spasmodic torticollis is a most intractable condition and in many cases temporary alleviation is all that can be secured It is usually best to begin treatment by rest in bed the patient lying supine with the head low and between sandbags or pillows The regular administration of phenobarbitone or of chloral and bromide may then be tried Many years ago Bastian claimed good and permanent results from a continuous narcosis lasting 3 weeks and induced by chloral hydrate Probably a combination of rest as above described together with massage and resistance exercises is the most useful line of treatment In some cases the application of a plaster mould fixing head and shoulders and worn for one or more months or a more easily removed and lighter metal splint will give complete respite from muscular spasm while it is worn and very occasionally permanent respite after removal In severe and disabling cases this is well worth trial Surgical measures (tenotomy excision of the sterno mastoid posterior root section) have all proved disappointing and are not to be recommended Except in cases of hysterical origin psychological treatment is without effect

There is a *congenital form of torticollis* which is of a very different nature The disease is prenatal and analogous to congenital talipes the sterno mastoid alone is affected and nearly always that of the right side Such a muscle is frequently ruptured during birth, and this has given rise to the opinion that the birth injury and subsequent hæmatoma of the muscle were responsible for the torticollis In many of these cases there is marked facial asymmetry the face being smaller on the side of the affected sterno mastoid This association points strongly to some defect in the nerve centres of the medulla Treatment consists in tenotomy of the contracted muscle

THE TICS

Synonym —Habit Spasm

Definition —A group of maladies characterised by the occurrence of (1) sudden rapid twitch like involuntary co ordinated movements always of the same nature and in the same region or of (2) sudden psychical phenomena imperative ideas and explosive utterances or (3) of a train of deliberate highly co ordinated actions produced by an imperative idea Any combination of these phenomena may occur

The tics are both ætiologically and clinically related to spasmodic torticollis into

which some of the motor tics gradate A torticollic movement may occur as a tic and it may in rare cases pass over into an established torticollis

The tics may be conveniently divided for clinical purposes into the following groups between which any combinations may occur

(1) The clinical picture is made up by the occurrence of sudden twitch like co ordinated movements which resemble reflex or defence movements The movement is always of the same nature and occurs in the same region though several different tics may occur in the same patient The usual region affected is the face with the pharynx and larynx the neck and upper extremity This form occurs chiefly in children and usually runs a favourable course—Simple Tic

2 The spasms are more severe and complicated than in simple tic and imperative ideas and explosive utterances are common and important symptoms The condition is met with soon after puberty and more commonly in males—Convulsive Tic

3 There is no spasm or other motor manifestation but the psychic tic is ex pressed by uncontrollable imperative ideas explosive utterances arithmomania etc — Psychical Tic

The tics are expressions of unrest and of embarrassment in consciousness in a nervous system which is highly sensitive and not too stable There is always the desire to relieve the embarrassment by the occurrence of the tic and a feeling of relief when it has occurred coupled often with disappointment at the failure of its sup pression

While the more simple forms of motor tic from their pattern suggest strongly that they were originally associated with some peripheral irritation from the con junctiva in the case of a blinking tic from the nose in a case of snuffling tic and from the larynx in a case of laryngeal tic and that constant irritation from these regions has set up a habit yet it cannot be too strongly pointed out that in many cases no such peripheral irritation precedes the onset of tic and the irritation and cause come from within the nervous system alone

1 SIMPLE TIC

Synonym —Habit Spasm

This is a common disorder of late childhood the majority of the cases occurring between the fifth and tenth year Both sexes are prone to the condition The onset may be preceded by deterioration of health from any cause and sometimes fright and emotion bring on the tic Often the malady arises in perfectly healthy children with out assignable cause The children are usually highly strung and intelligent It is a rare event to see a dull and backward child with a tic

Symptoms —The recurring tic appears somewhat suddenly and may reach its height in a few days The movements are of the nature of a simple act They occur *suddenly and without warning and are executed rapidly Usually the movement* is of one kind only but sometimes several movements coexist The common site of the spasm is the head face and neck Blinking winking alternate elevation and depression of the eyebrows side to side movements of the mouth tossing the chin in the air sudden movements of the tongue palate or larynx accompanied by an unpleasant fidgeting sound are of frequent occurrence while any movement of the head upon the shoulder torticollic movements shrugging of the shoulder and any movements of the arm may be met with Respiratory movements are often associated with those occurring in the tongue and larynx Tic affecting the legs is much less common The movements cease during sleep Generally a variable time of some length separates the individual movements but in severe cases these may follow one another almost unceasingly They are increased by excitement and by observation and can usually be controlled by the will but only for a limited time

Diagnosis —The movement of tic is so peculiar that it cannot be confused with

any other spontaneous involuntary movement It is the same movement repeated with very rapid execution in the same place It is short and sharp like a twitch In chorea the movements are slow compared with those of tic and are irregular in nature in time and in place

Prognosis —Most cases of simple tic recover whether they are treated or not. They recover much more quickly under treatment and 2 or 3 months suffices in most cases to see the end of them The longer a tic lasts the more difficult it is to cure In the rarest cases only does a tic of this nature persist or merge into one of the more severe forms

Treatment —A scrutiny of the general health should be made and any defects attended to Matters of hygiene diet, education, exercise and pleasure should be correct and normal Observation and remarks upon the child s defects and anything tending to increase self consciousness should be avoided The confidence of the child should be gained if possible and any source of mental worry or grief or annoy ance should be ascertained and corrected Restraint and discipline should be kindly taught, and an orderly life followed in which the child is happy, and in which his time is fully and congenially employed

2 CONVULSIVE TIC

In this malady which was first described by Gilles de la Tourette and which bears his name the same movements as are met with in simple tic occur but they are more severe and more widely spread and they may involve the whole body in spasm at one time In addition there are psychic tics which cause irresistible im pulses among which are explosive utterances repetition of words sounds and gestures, and also imperative ideas

Ætiology —The stigmata of physical and mental degeneracy are rarely absent neuropathic and sometimes direct heredity is often present The malady is said to be more common in males and is met with more often in France than in England—*where it is a rare disorder The symptoms appear usually between the ages of* 10 and 15 years and commonly follow physical or mental shocks or acute illness of any kind

Symptoms —The spasmodic movements resemble at first those of simple tic in their nature and rapidity and favour the same sites but they are not restricted to the repetition of the same movement but successive movements may vary widely *in position* and extent and sometimes involve the whole musculature of the body The great variety of facial grimaces head jerking grotesque attitudes and ridiculous pantomime which may occur in this affection lead commonly to the belief that the patient is shamming The tic is not continual as in the simple form It occurs in the form of bouts in which the same pantomime is reproduced These are often excited by observation and emotion They can often be controlled but with much *fatiguing effort on the part of the patient* who becomes so worn out with half successful efforts to control them that he ceases to make the attempt Between the attacks the patient seems quite normal The psychic phenomena are the same as in psychical tic about to be described and the treatment of the two conditions is identical

3 PSYCHICAL TIC

In this condition there is no muscular spasm but the sudden event takes the form of explosive utterances imperative ideas and impulsive acts This condition often occurs as a part of convulsive tic The exclamatory tic consists of some sound or word or group of either which is habitually uttered with complete irrelevancy of time place or sense Sometimes the words are of an obscene nature and cause the greatest distress to the patient The utterances may be single or may be repeated

over and over in rapid succession Echolalia which is an uncontrollable impulse to repeat sounds heard or to repeat words which the patient or others have just spoken may be met with The great characteristic of the condition is that though the patient desires above all other things to prevent their occurrence he cannot do so by any effort of will Other symptoms that are commonly met with in this condition are imperative ideas and impulsive acts of all sorts and in general the symptoms of a severe obsessional state

Diagnosis —Both in the convulsive and psychical tics the diagnosis is placed beyond doubt both by the nature of the movements and by the peculiarity of the psychic disturbance

Prognosis —Permanent recovery has occurred from both these conditions but such an event is rare Most of the cases follow a downward course despite treatment and many end in suicide or insanity

Treatment —General tonic treatment with change of circumstance and healthy pursuits and congenial intellectual and physical occupation are the most likely to benefit The psychiatric treatment is that of the underlying obsessional state

OCCUPATION NEUROSES

Synonyms —Craft Palsy Occupation Palsy Occupation Cramp

Definition —A peculiar malady determined by the habitual use of one set of muscles for the constant repetition of an act of short range to the exclusion of acts of wider range and acts involving a different set of muscles The symptoms are (1) local pain in the muscles concerned, (2) local spasm of the muscles (3) loss of volitional control of the range and nature of the movements and (4) weakness of the movements These symptoms may occur separately or together

Ætiology —The variety of names by which this group of disorders has been known reflects the uncertainty and change in views as to its ætiology and patho genesis Certain facts are however generally agreed (1) The disorder is apt to arise in any occupation involving rapid repetitive movements of short range by a small portion of the body especially the hand Such movements figure prominently in the occupations of manual writers typists telegraphists musicians seamstresses and many others The movements concerned are always acquired and necessitate a high degree of precision and co ordination but in the course of time become so automatic that in health they are carried out without attention and almost subcon sciously while the performer s thoughts are concentrated on other aspects of his work (2) They involve the rapid repetitive action of small groups of muscles which may thus be supposed to be subject to especial fatigue In many such occupations from 5 to 10 repetitive movements a second may be executed (3) No structural change in the cerebral cortex nervous system or muscles has ever been demonstrated (4) In the vast majority of cases the disability initially concerns only one set of stereo typed movements and the affected parts function normally in other activities even though these involve movements of comparable rapidity and skill Thus the subject of writer s cramp is able to use the hand normally for shaving eating or even for playing the piano In severe and intractable cases however other similar co ordinated movements of the hand may gradually be drawn into the ambit of the disorder especially if they concern the patient s definitive occupation (5) The first manifesta tions of the disorder are likely to make their appearance when the individual is called upon to exceed a certain level of performance or after any physical or psychological event which may lower the patient s normal level of efficiency (6) The more searching the enquiry the greater is the number of these cases that are found to show evidence of predisposition towards psychological instability In a study of telegraphist s cramp in 1927 this was estimated to be as high as 75 per cent (7) Faulty training in the

any other spontaneous involuntary movement It is the same movement repeated with very rapid execution in the same place It is short and sharp like a twitch In chorea the movements are slow compared with those of tic, and are irregular in nature in time and in place

Prognosis —Most cases of simple tic recover whether they are treated or not They recover much more quickly under treatment, and 2 or 3 months suffices in most cases to see the end of them The longer a tic lasts the more difficult it is to cure In the rarest cases only does a tic of this nature persist or merge into one of the more severe forms

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Symptoms —The spasmodic movements resemble at first those of simple tic in their nature and rapidity and favour the same sites but they are not restricted to the repetition of the same movement but successive movements may vary widely in position and extent and sometimes involve the whole musculature of the body The great variety of facial grimaces head jerking grotesque attitudes and ridiculous pantomime which may occur in this affection lead commonly to the belief that the patient is shamming The tic is not continual as in the simple form It occurs in the form of bouts in which the same pantomime is reproduced These are often excited by observation and emotion They can often be controlled but with much fatiguing effort on the part of the patient who becomes so worn out with half successful efforts to control them that he ceases to make the attempt Between the attacks the patient seems quite normal The psychic phenomena are the same as in psychical tic about to be described and the treatment of the two conditions is identical

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disabling fashion In a third and numerous group it progresses to incapacity, and tends to reappear with every change of occupation In a few cases the patients become incapacitated for all the finer movements of both hands The prognosis is usually serious but a correct forecast can only be made from the history and progress of each individual case

Treatment—The responsibility and costliness which the Compensation Act entails upon employers are slowly enough but surely leading to the abandonment of those instruments the manipulation of which may produce cramp Good teaching of unconstrained methods of manipulation and encouragement of ambidexterity in all the occupations concerned are important prophylactic measures Long hours and the speeding up of work should be avoided After long absence from work the work should be gradually resumed and not recommenced at full pressure When the malady appears rest and change of work afterwards are absolutely essential Long continued rest be it remembered cuts both ways for, as has been pointed out above resumption after long rest is actually a cause of cramp for long unemployment decreases the stability and the aptitude of the mechanism

General treatment consists of the removal when possible of adverse factors in the patient s environment such as uncomfortable working conditions poor light excessive noise and sources of personal friction Full attention should be given to all aspects of the subject s physical well being

Psychological treatment may play a valuable part in relieving the underlying anxiety and tension and in enabling the individual to make a better adaptation to his surroundings and whenever necessary in giving guidance as to a change in occupation Careful selection of personnel in occupations liable to the disorder is of great value in eliminating those with special predisposition to this form of breakdown

When attention has been given to these factors re education of the movements themselves can profitably be attempted particularly in the variety of the disorder most often encountered in general practice—namely writer s cramp A specially large pen or pencil should be used and held loosely and comfortably in the natural writing po ture At first the patient should practise drawing straight lines from left to right with easy movements of the forearm Next while the same basic movements are maintained the lines should be made wavy by simultaneous movements of the wrist Then the waves should be regularly interrupted so that they become series of pot hooks m s and n s From this by gradual stages the smooth execution of other letters may be achieved

LOCAL LESIONS OF THE SPINAL CORD

INTRODUCTION

For le ions of the spinal cord the general rule applies that examination of the nervous system enables us to determine the nervous structures which are affected and also the site of a lesion but in order to determine the nature of the lesion we are dependent on information obtained from other sources namely (1) the history (2) the general examination of the patient and (3) special tests

There are many morbid affections in which the spinal cord is damaged only in a short portion of its extent and it may be of the greatest importance to determine the exact site of the lesion

The functions of the motor and sensory tracts are usually to a greater or less degree interrupted by the lesion and it is possible by examination of these functions to determine the somatic level below which muscular weakness spasticity and reflex disturbances exist and below which sensory functions are impaired By these means

use of the instrument, *e g* the pen, and bad design in machinery, *e g* certain varieties of Morse transmitters predispose to the disorder in operatives concerned

Opinion has gradually moved away from the original conception that the disorder was due to structural change or uncomplicated physical fatigue towards the view that it is primarily psychogenic Causative factors are no doubt numerous and often multiple and both physical and psychological in nature but in their summation they result in the breakdown of the smooth execution of a stereotyped movement and ultimately lead to the setting up of a faulty habit closely akin to a stammer or a tic.

Symptoms —These are of two orders namely subjective consisting of dis comfort pain and the sense of fatigue and objective comprising muscular spasm and the abnormalities of movement arising from it and from the effort to avoid both pain and spasm In some subjects pain in others spasm predominates

The onset is gradual In the case of writer s cramp the movements of the pen become inexplicably difficult and tend to be irregular, the strokes extending too high or too low The subject then finds himself grasping the pen with excessive force and the correct adjustment of the finger ends becomes hard and apt to fail the index slipping off the penholder This he tries to correct by a still firmer grasp The hand then begins to ache, and feels heavy and tired With the passage of time all these symptoms increase and the writing becomes more irregular and the nib is driven more firmly into the paper which it penetrates the ink spluttering over the sheet Some tremor may develop in the limb As the condition grows worse the cramp appears more and more readily when writing is started, so that even taking the pen in the hand may evoke cramp At the same time other fine and repetitive movements of the hand may be performed with normal ease and facility The pain which in varying degree accompanies the cramp tends as the affection grows worse to spread from the small hand muscles up the limb until the whole arm and shoulder ache With variations dependant upon the details of the movements involved comparable disturbances are seen in the other varieties of the disorder

Diagnosis —From what has been said of the character of the symptoms in these forms of cramp of the mode of their production by a particular movement complex and of their occurrence in the absence of signs of organic nervous disease it seems reasonable to state that errors of diagnosis should not occur

Nevertheless errors are not infrequent and consist in the diagnosing of writer s or of telegraphist s cramp when in fact some organic affection is present Paralysis agitans with little or no tremor and post encephalitic Parkinsonism provide fruitful sources of error In the clinical picture thus presented the initial symptoms may involve the right arm and hand and at first consist in a difficulty in the normally rapid and free performance of fine movements Not unnaturally the handwriting may be affected early It becomes slow in performance spidery and progressively smaller and the effort to continue writing may be irksome and even painful The total clinical picture in such a case is made up of such small deviations from the normal that the inexperienced or careless observer may miss them and may note no more than the patient himself has noted namely that it has become difficult and un comfortable to write Amongst other organic conditions which may be encountered under the erroneous diagnosis of writer s or telegraphist s cramp may be included cervical rib any organic nervous affection which impairs fine hand movements arthritis and painful affections of muscles The general principle which underlies accuracy of diagnosis here as elsewhere is careful and systematic clinical examination

Course and Prognosis —In a young subject who shows signs of the malady during training or soon thereafter the outlook is hopeless with regard to continuance of the occupation and the progress is from bad to worse In older subjects the course varies greatly Some cases recover completely and permanently even though they continue with the occupation In others—and this class is much larger than is usually supposed—the condition of cramp becomes stationary and persists though not in

kind of movement appears in which the limbs are drawn up suddenly from time to time by an involuntary contraction of the flexor muscles—flexor spasms Further by appropriate stimulation many reflex movements can be produced in the paralysed limbs The most important of these is the flexion reflex of the lower limb This is elicited most easily by stimulating the outer border of the sole by firm pressure or a pin prick and in its complete form consists in flexion of the hip and knee dorsi-flexion of the foot and an upward movement—so called extension but physiological flexion—of the great toe When the damage to the motor tracts is slight when the limbs are rigid in extension and the movement of flexion is prevented by the hyper tonus of the extensors or when almost all reflex activity has disappeared the reflex appears in its minimal form A part of this minimal response is an extension of the great toe The normal flexor plantar response is obtained from the sole alone The pathological reflex of which the extensor response is a part, may be obtained not only from the sole but when well developed by stimulating the skin and deeper structures on any part of the lower limb In the light of this the nature of many reflexes which have been described as isolated signs of pyramidal tract disease *e g* the extensor plantar response Oppenheim s and Gordon s signs and many others become clear In all of them a stimulus is applied to some part of the lower limb and the response is a flexion reflex whose most obvious component is extension of the great toe It is unfortunate that the term extensor response is commonly used to describe a movement which is physiologically one of flexion

SENSORY TRACT DISTURBANCES

The level of the lesion may be determined approximately by ascertaining the highest point at which sensation is impaired but in general for reasons which will be given the exact site of the lesion is usually several segments higher than the level determined by this method When the two sides of the cord are affected unequally the anæsthesia is confined to one side or extends higher on one side than on the other In many instances reliance has to be placed on the disturbances of pain and tempera ture sensation and it must be borne in mind (1) that the spino thalamic tract in the antero lateral column of the cord is concerned with pain and temperature sensation on the opposite half of the body and (2) that the fibres crossing the cord to join it do so with different degrees of obliquity at different parts of the cord In the lumbo sacral enlargement the pain and temperature fibres cross slowly and in fact clinical experience suggests that they have not taken up their new position until they reach the twelfth dorsal segment In the mid dorsal region the decussation of pain and temperature fibres is complete one segment above the point of entry of the root by which they reach the cord At higher levels crossing again takes place more slowly until in the upper cervical region impulses which enter together in one root ascend through five or six segments before all of them reach the opposite side At all levels pain crosses most quickly then cold then heat and touch slowest of all

When the posterior columns of the cord are involved in the lesion loss of sense of position occurs in the feet and legs with resulting ataxia Disturbances of posterior column sensation cannot be used for localisation in the dorsal portion of the cord but in the cervical portion the disturbances of postural sense in the different fingers may be of localising value

BROWN SÉQUARD SYNDROME

When a lesion affects one half of a segment of the spinal cord it interrupts (1) the pyramidal tract conveying motor impulses for the lower limb on the same side and (2) the spino thalamic tract conveying pain and temperature impulses from the opposite side of the body below the level of the lesion and (3) the posterior column conveying sense of position impulses from the lower limb on the same side as the

the level of the lesion can be determined approximately Secondly, the motor sensory and reflex functions of the individual segments of the cord are known and from this knowledge it is possible to determine more precisely in which segments of the cord function is abolished or impaired and therefore at what precise level the lesion is situated Myelography (p 1533) may confirm the site of the lesion and gives additional information in very many cases

MOTOR TRACT DISTURBANCES—SPASTIC PARAPLEGIA

Motor symptoms —Interruption of the pyramidal tracts produces spastic weakness in parts below the lesion which when fully developed, constitutes the picture of *spastic paraplegia The clinical features are* (1) Diminution of voluntary power (2) alterations in the amount and distribution of muscle tone and in the attitude of the limbs (3) changes in the tendon and skin reflexes and (4) the occurrence of certain involuntary and reflex movements

The phenomena of spastic paraplegia have been analysed by Walshe as follows it is essential to remember that the muscles of the lower limb are divided into two distinct groups, namely the flexors and the extensors and that the muscles which dorsiflex the foot and toes are physiologically flexors while the corresponding plantar flexors are extensors In all that follows these important muscles will be grouped according to this nomenclature

1 Loss of voluntary power varies from slight weakness of one group of muscles *to complete paralysis of both limbs and depends on the degree of damage to the* pyramidal tracts It usually begins in the distal segments of the limb and is greater in the flexors than in the extensors Dorsiflexion is the earliest and remains the most severely impaired movement

2 The tone in all the muscles increases early and is greatest in the extensors Hence an early symptom is generally stiffness of the limbs especially a difficulty in flexing them If the limbs are handled passively the resistance to flexion is found to be greater than to extension It is greatest at the beginning of a passive movement and decreases suddenly in a way that has given rise to the expression clasp knife rigidity As power diminishes spasticity increases, until at length the limbs are held constantly in an attitude of complete extension This combination of weakness *and spasticity with extended lower limbs is known as* paraplegia in extension

As the damage to the cord increases and when certain extra pyramidal motor tracts are affected *the extensor muscles gradually lose their excessive tone for which* connections with the brain stem through these extra pyramidal tracts are essential while the tone in the flexor muscles which depends *on a reflex arc which is purely* spinal is retained The result is that the knee and ankle jerks which indicate tone in extensor muscles are lost while the reflexes from flexor muscles (hamstring jerks) persist At the same time in some cases the limbs are gradually drawn up by the unopposed action of the flexors This combination of weakness and spasticity with flexed lower limbs is known as ' paraplegia in flexion At first the flexed position is occasional—flexor spasms later it becomes constant but is still due entirely to excess of tone in the flexors and ultimately contractures occur in the muscles and the deformity becomes permanent

3 Exaggeration of the tendon reflexes is a constant early sign of spastic paraplegia The abdominal reflexes below the level of the lesion and the cremasteric reflexes are lost early The normal plantar reflex is also lost and is replaced by a different kind of reflex—Babinski s sign the extensor plantar response

4 While the limbs are still rigid in extension the commonest involuntary movement is a spontaneous clonus of the extensor muscles in which the whole limb trembles as it does when ankle clonus is elicited in a case with marked spasticity In the later stages when the extensor muscles are beginning to lose their tone a new

segments between the "root loss" at the affected site and the upper limit of the "tract loss" In many other cases there is a state of hyperalgesia in the segmental areas corresponding to the segment just above the lesion or to the affected segment itself if the lesion be a relatively slight one

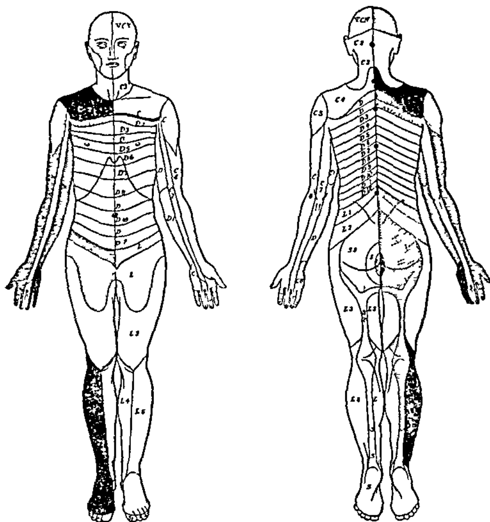


FIG 3 —Diagram of cutaneous areas of posterior nerve roots

DISTURBANCES OF THE BLADDER AND RECTUM

Emptying of the bladder is essentially a reflex function but in the normal state the reflex is voluntarily controlled being inhibited or initiated at will The detrusor musculature of the bladder wall is innervated by para sympathetic fibres from the second and third sacral segments of the spinal cord through the vesical plexus The sphincter musculature is also innervated by the sacral nerves as well as by sympathetic fibres coming from a higher level namely from the first and second lumbar seg ments with contributions from the third and fourth The emptying reflex is excited

lesion Consequently a local lesion affecting one half of the cord produces a syndrome, described by Brown Séquard, consisting of loss of power (with spasticity) on one side and loss of pain and temperature appreciation on the other side below the level of the lesion and if the posterior column is involved (and it often is not) loss of sense of position on the same side as the weakness

The Brown Séquard syndrome most commonly results from lesions in the thoracic portion of the cord Occasionally it occurs with lesions in the cervical portion, and then the upper limbs as well as the lower may be involved It does not occur with lesions in the lumbar or sacral cord because as has already been mentioned the pain and temperature fibres have not crossed in these portions and consequently with lumbar and sacral unilateral lesions all the sensory loss is on the same side as the weakness

SEGMENTAL DIAGNOSIS

Motor localisation —Each segment of the cord contains groups of anterior horn cells for several muscles and most muscles receive nerve fibres from more than one root but as each muscle seems to have one main root of supply the weakness wasting and loss of tone vary in distribution with the segment affected The muscles which suffer most when the corresponding segment is damaged are named hereunder

> C_4 *Supraspinatus infraspinatus* C_5 *Biceps deltoid brachialis supinator longus* C_6 Pronators of forearm C_7 Triceps extensors of wrist and fingers C_8 Flexors of wrist and fingers D_1 Small muscles of the hand $D_{2\,10}$ Intercostal muscles $D_{7\,12}$ Muscles of the abdominal wall $L_{2\,3}$ Adductors of thigh L_4 Abductors of thigh extensors of knee L_5 Hamstrings—Anterior tibial muscles S_1 Glutei—calf muscles S_2 Anterior tibial muscles—peronei—small muscles of foot

Wasting of the muscles in an intercostal space is a valuable guide as the muscles of each space are innervated from one segment alone If the lesion is at the level of the ninth dorsal segment the rectus abdominis is weakened below a point about an inch above the umbilicus In such a case when an attempt is made to raise the head against the resistance of a hand placed on the forehead when the patient is in the supine position the upper part contracts and the umbilicus is drawn upwards (excursion of the umbilicus) If the lesion is at the twelfth dorsal segment the entire rectus contracts but the iliac regions bulge owing to weakness of the lower part of the oblique muscles

Localisation by changes in the reflexes —Above the lesion the reflexes are normal at its level they are diminished or lost below it the skin reflexes are diminished or lost and the tendon reflexes are exaggerated The segments on which important reflexes depend are

> C_5 Biceps and supinator jerks C_6 Pronator jerks C_7 Triceps jerks $D_{7\,12}$ Abdominal reflexes L_2 Cremaster reflexes $L_{3\,4}$ Knee jerks S_1 Ankle jerks S_1 *Plantar reflexes*

In lesions involving the fifth cervical segment of the cord such as may be found in syringomyelia and in injuries associated with dislocation of the cervical spine Babinski has recorded that the supinator jerk may be abolished and replaced by finger flexion when the lower end of the radius is tapped This is known as inversion of the radial reflex and is a useful localising sign of lesions of the segment in question

Sensory localisation —The sensory areas supplied by each segment of the cord are shown in the diagrams on p 1531 Root pains in the distribution of one or more of these areas form a fairly sure guide to the affected segment There may also be sensory loss or impairment over the same areas and this may be continuous below with the sensory loss which is the result of interference with the sensory tracts or there may be an interval corresponding to the distribution of one or several

and the first sacral segment at the level of the twelfth The cord terminates just above the level of the first lumbar spine

LOCALISATION BY MYELOGRAPHY

When the existence of a compressive lesion of the cord or its exact site is in doubt great help may be obtained by injecting into the thecal canal a fluid substance which is opaque to radiography If 1 or 2 ml of Myodil or other opaque medium be injected through the occipito atlantoid ligament into the cisterna magna of the sub arachnoid space it falls rapidly to the site of obstruction where it is arrested wholly or partially and can be seen on the radiographic screen or film in relation to the vertebræ A safer procedure is to inject the Myodil by lumbar puncture and then making use of a tilting X ray table to tilt the patient so that the oil runs towards his head Even when the lesion is as high as the cervical region this manœuvre is satisfactory though some discomfort may be caused to the patient by prolonged tilting The oil will run more rapidly within the theca if it is heated to just above body temperature by immersion of the phial in warm water for 15 to 20 minutes before injection

GENERAL MANAGEMENT OF PARAPLEGIA

In all cases of severe paraplegia from spinal cord lesion in which sensory and sphincter functions are also impaired or lost whatever the nature of the lesion there are certain general principles of treatment The patient should be nursed on a fracture bed with an air water or foam rubber mattress The back should be attended to 4 hourly first washed with soap and water then carefully dried rubbed with surgical spirit or Eau de Cologne and powdered These measures harden the skin and make it less likely to break down under the constant pressure of the body-weight The patient s position should be changed at intervals of not more than 3 hours and he should be made to lie on his face for at least 6 hours in 24 in order to prevent the development of sacral bed sores When there is incontinence of urine as far as possible care should be taken to prevent the skin from becoming wet and sodden and the toilet of the anus after defæcation should be careful and thorough There are various remedies for the sacral or trochanteric bed sore when it develops Separation may be hastened by wet dressing of eusol or sometimes by fomentations though the latter should be used with caution The ulcer is packed with eusol gauze or with an ointment of zinc oxide and castor oil When it is clean and healing begins it may sometimes be hastened by dressings of gauze soaked in red lotion The heels should also be carefully watched for the appearance of the hæmorrhagic blisters which herald the development of a sore Rings for the heels may avert them and air rings for the sacrum may also be needed

Rehabilitation of the paraplegic —Experience gained during the War of 1939–1945 has gone far to improve the lot of paraplegics suffering from irreparable but solitary lesions of the spinal cord particularly young subjects with traumatic lesions

Bed sores even of large dimensions can be caused to heal by active treatment as described by Guttman Supra pubic cystotomy and tidal drainage of the bladder may gradually be replaced by the development of satisfactory automatic emptying which permits the use of a urinal Contractures and deformities can be prevented or where necessary corrected Physiotherapy and training directed to the healthy muscles may enable the patient to replace to a great extent the functions of the paralysed parts as well as overcoming the gravitational effects in the circulation which are a conspicuous feature of thoracic cord lesions

Finally occupational therapy, both prevocational and vocational in specialised spinal centres and mental readjustment can enable these patients to a remarkable degree to resume their places as active members of the community

by an appropriate degree of pressure within the bladder and it evokes a co ordinated activity combining contraction of the detrusor with relaxation of the sphincter Voluntary control over this reflex is exerted through the upper motor neurones, and as long as one pyramidal tract is functioning perfectly control of the bladder remains normal When the function of both pyramidal tracts is impaired by a spinal lesion above the lumbar region voluntary inhibition and voluntary initiation of the bladder emptying reflex become imperfect If spinal reflex activity below the level of the lesion is greatly exaggerated as for instance in many cases of disseminated sclerosis the bladder emptying reflex is hyper active and with the impaired control the patient is unable to inhibit it and precipitancy of micturition results In other instances the patient is unable to initiate the reflex when he wishes and may be able to pass urine *only after long delay* While one or other form of disturbance usually predominates they are not mutually exclusive and both may occur on different occasions in the same patient Delay in micturition may go on to retention as a progressive spinal lesion becomes more complete

With sudden or rapidly occurring tract lesions above the lumbar region associated as they are with depression of spinal reflex activity retention of urine is the rule As soon as the bladder becomes distended retention is followed by overflow incontinence and it should be an invariable rule in all cases of incontinence to feel for a distended bladder in the abdomen At a later stage in many such cases spinal reflex activity increases and reflex emptying of the bladder may then occur at intervals The bladder may act spontaneously or the reflex may be initiated by pressure on the lower abdomen or by other means Such reflex micturition is a useful aid in the management of a case of complete paraplegia but it should be realised that emptying of the bladder by this means is always incomplete and leaves a considerable amount of residual urine

With lesions in the upper lumbar region of the cord the vesical sphincter is paralysed and dribbling incontinence results Lesions in the second and third sacral segments or in the corresponding spinal roots interrupt the arc of the emptying reflex and so cause retention with a flaccid condition of the bladder wall Lesions in the conus medullaris where there is a reflex controlling centre, produce the same effect

Control of the rectum is in nearly every respect similar to that of the bladder Incontinence of fæces usually occurs only after aperients have been taken retention expresses itself as constipation and may be relieved by regular enemata

SWEATING

With severe lesions of the spinal cord sweating is excessive on the paralysed parts of the body If not evident it may be excited by cutaneous stimuli or by the injection of a small dose of pilocarpine (gr $\frac{1}{6}$) and the level of a spinal lesion may be determined by this means by an observer who is familiar with the cutaneous segmental distribution

SURFACE ANATOMY

If the cord is to be exposed at the level of the affected segments their relation to the spinous processes of the vertebræ must be known The segmental localisation of a lesion having been obtained the desired segment can be found as follows in the cervical region of the cord deduct one from the number of the segment—the sixth cervical segment is at the level of the fifth cervical spine in the upper half of the thoracic cord deduct two—the fifth thoracic segment is at the level of the third thoracic spine, and down to the first lumbar segment deduct three—the first lumbar segment is at the level of the tenth thoracic spine The remaining segments of the cord are shorter and so are farther separated from their corresponding vertebræ The third lumbar segment is approximately at the level of the eleventh dorsal spine

Localised spinal syphilis may also closely simulate intramedullary tumour but such cases are quickly recognised if the Wassermann reaction is performed on the cerebrospinal fluid and blood as a routine measure

The diagnosis between intramedullary tumour and compression of the cord from without (*e g* by a meningeal tumour or a neurofibroma) cannot usually be made with confidence on clinical grounds Search should first be made for evidence of those conditions which are known to cause compression Queckenstedt s test may of course indicate obstruction in the theca but in many cases at the stage at which diagnosis is called for it gives an indefinite result and radiographic investigation with Myodil is then required If this reveals no obstruction or if the picture obtained indicates a fusiform expansion of the cord with a little of the oil passing down at the sides of it the diagnosis of intramedullary tumour may be accepted In many cases the final diagnosis is made only by exploratory operation

Treatment —Many ependymomas have been successfully removed by skilled neuro surgeons the cord having been incised between the posterior columns If exploratory operation reveals a glioma or evidence of a hæmangioma surgery can do no more to benefit the patient and the treatment thereafter is that of paraplegia in general Radiotherapy is ineffective

COMPRESSION OF THE SPINAL CORD

In compression the lumen of the spinal canal is reduced in a small part of its length and the spinal cord is injured at this point either directly by pressure or indirectly by interference with its blood supply Nearly all the extramedullary lesions of the cord come under this heading Except in cases of collapse of a vertebral body such as may occur in malignant disease compression is in general a slow process although in a number of cases the symptoms come on rather abruptly A sudden process such as fracture dislocation of the spine causes laceration rather than compression of the cord

Clinically compression is characterised by a combination of two sets of phenomena namely, local or root symptoms in the regions supplied by the roots arising from the cord at the level of the lesion and remote or cord symptoms due to interruption of the conducting paths in the white matter Obstruction of the spinal theca may be inferred if Queckenstedt s test (see p 1378) is positive In addition complete or partial obstruction is associated with an increase of protein in the fluid below the obstruction and Froin s syndrome (see p 1379) may be present In most cases the fluid shows a slight degree of xanthochromia Radiographic examination after injection of Myodil into the theca (see p 1533) confirms or reveals the site of the obstruction and the outline of the filling defect may give a valuable clue to its nature

Compression of the spinal cord may be the result of (1) conditions arising within the theca the most important of these being meningeal tumours neurofibromata and arachnoiditis and (2) lesions compressing the theca and subsequently the cord Of the latter the most important are vertebral diseases especially tuberculous disease of the spine and secondary carcinoma also common is a protruding intervertebral disc and rarer causes are extra thecal abscess Hodgkin s disease Paget s and other forms of bone disease

I INTRATHECAL COMPRESSION

MENINGEAL TUMOURS

Though fibroma and sarcoma are occasionally found for practical purposes the meningioma or endothelioma of the dura is the only common tumour arising from the spinal meninges

TUMOURS OF THE SPINAL CORD

Synonym —Intramedullary Tumours

Ætiology and Pathology —Tumours of the spinal cord while uncommon are not rare and are encountered at all ages According to Kernohan s statistics the ependymoma a tumour arising from the cells of the ependyma of the central canal is the commonest type forming about half of the total number Tumours of this variety are demarcated from the nervous tissue of the cord, and although centrally placed are capable of surgical removal They arise most frequently in the cervico thoracic region and in the filum terminale Various types of gliomata form the remainder of the total the glioblastoma being the most common all the tumours of this group are of an invasive character devoid of any definite demarcation and therefore incapable of being removed by operation without gross damage being done to the cord In addition to the tumours arising from the tissues of the cord medulloblastomata and oligodendrogliomata may be found on the surface of the cord as seedling metastases from cerebral and especially cerebellar tumours Various types of hæmangioma are also found

Symptoms —In the case of any patient presenting the signs of a local lesion of the spinal cord of gradual onset the possibility of an intramedullary tumour should be kept in mind

The symptoms often start unilaterally, with weakness and stiffness of one leg and at a slightly later stage a partial Brown Séquard syndrome is not uncommon At all stages dissociated sensory disturbances are common on account of different degrees of involvement of sensory tracts Root pains are unusual but local muscular wasting corresponding to one or several consecutive segments is frequently present Sphincter disturbances occur at a relatively early stage

The cerebrospinal fluid contains a moderate excess of protein and some excess of globulin Queckenstedt s test does not indicate any blockage in the spinal theca until the tumour has reached such a size that it occupies most of the width of the theca Unless the tumour is at an advanced stage there may be no obstruction to the passage of Myodil and even at a late stage the obstruction may be only partial The expanding mass within the spinal theca may cause thinning of the pedicles of several consecutive vertebræ which may be apparent in the radiograph and in consequence of the thinning the interpeduncular distance on each affected vertebra is increased

Diagnosis —This has to be made from (1) other forms of spinal cord disease which produce paraplegia of gradual onset and (2) compression of the cord from without Of the former disseminated sclerosis is usually the most difficult to exclude and is the disease to which the symptoms of spinal tumour are most often wrongly attributed The diagnosis of disseminated sclerosis is rarely justified unless there is evidence of several lesions in the central nervous system and if after careful examination of the whole nervous system all the signs and symptoms can be attributed to a single spinal lesion the probability of tumour is greatly increased Secondly with tumour the exacerbations and remissions of disseminated sclerosis do not occur Finally in a case of tumour the cerebrospinal fluid may show a considerable increase of protein a moderate increase however (06 per cent or less) does not help in the differentiation It should also be borne in mind that the spinal fluid in an active case of disseminated sclerosis occasionally gives a paretic type of curve with Lange s colloidal gold test, which does not occur in the case of tumour Cases of supposed disseminated sclerosis beginning after the age of 45 especially in males should be regarded with the greatest suspicion The diagnosis may be particularly difficult in cases of hæmangioma of the cord because in many of these there is evidence of two spinal lesions

may not give rise to severe symptoms A neurofibroma may be situated partly within and partly outside the vertebral canal the constriction at the intervertebral foramen giving the tumour a dumb bell shape Histologically the intrathecal neurofibroma has a structure similar to that of the acoustic neuroma (see p 1382)

Symptoms —A neurofibroma compressing the spinal cord is apt to give rise to unilateral symptoms and to the Brown Séquard syndrome Root pains may be severe and in some cases there are spasms of intense pain on the opposite side of the body below the level of the tumour resulting from irritation of the spino thalamic tract by the growth

Diagnosis —The unilateral nature of the spinal signs may suggest the nature of the tumour Also neurofibromata cause a great increase of protein in the cerebrospinal fluid findings above 1 per cent are common in the lumbar fluid and even in the fluid above the tumour the protein content is raised The fluid withdrawn at lumbar puncture may be yellow Queckenstedt s test and examination with Myodil disclose complete or partial obstruction of the theca Radiographic examination of the spine shows in many cases enlargement of the intervertebral foramen through which the affected nerve root emerges and the Myodil picture may show the lateral situation of the obstructing mass

Prognosis and Treatment —For the solitary neurofibroma these are similar to those of a spinal meningioma When multiple neurofibromata are present the prognosis is less favourable although the removal of a single tumour may completely relieve the spinal compression

ARACHNOIDITIS

Synonym —Meningitis Serosa Circumscripta

Ætiology —As a result of a low grade inflammation of the arachnoid membrane adhesions occur within it and give rise to cystic formations containing cerebrospinal fluid or the membrane thickened and fibrous may become bound down on to the spinal cord Such arachnoiditis follows injury (perhaps as a reaction to hæmorrhage) or is a consequence of generalised infectious diseases or it may follow meningitis

Symptoms —In the course of a year or several years the cyst or contracting membrane may cause slowly increasing pressure on the cord Root pains are seldom pronounced but muscular wasting may occur corresponding to the site of the maximal local incidence of the arachnoiditis The tract signs are usually limited to gradually increasing spasticity of the lower limbs but sensory changes with a definite level may develop Pressure measurements at the time of lumbar puncture may reveal complete or partial obstruction of the theca and the Myodil picture may show an appearance of guttering the opaque fluid being broken into droplets among the arachnoid adhesions

Prognosis and Treatment —In the case of a cyst its removal by operation may bring about great improvement in the patient s clinical condition The sites of ad hesion may be difficult to see and if the cyst be opened inadvertently during operation the only evidence of its former presence is flattening of the cord and of the nerve roots at the level of the expected lesion Sometimes the position of the cyst can be inferred from the absence of normal pulsation below that level When the membranes are punctured in this position fluid escapes under pressure and the pulsations reappear Later symptoms may recur or in spite of operation they may progress as a result of the adhesive process

2 EXTRATHECAL COMPRESSION

With extrathecal compression the pressure on the spinal cord is apt to be more uniform and the manifestations have in consequence a greater tendency to be equal

Ætiology and Pathology—The meningioma is a firm oval pinkish tumour of smooth or nodular outline When impregnated with calcareous deposits the term psammoma was applied to it and it may become so calcified as to be discernible on a radiograph of the vertebral column The incidence of these tumours is mainly between 30 and 60 years of age and they affect women much more often than men Their common site is in the thoracic region and they usually lie posterior to the spinal cord

Symptoms—Pain of root distribution and of variable severity is usually the first symptom It is aggravated typically by coughing sneezing or straining This is followed after some time by spastic paralysis of slow onset and steady uninterrupted progress affecting first one leg and then the other the combination and especially the course of these symptoms being almost pathognomonic Sensory signs of similar slow course accompany the motor signs or follow them after a brief interval The sense of position may be the first to be disturbed and give rise to unsteadiness in walking and standing By the time the patient comes under observation the cerebro spinal fluid shows considerable increase in its protein content and in the globulin fraction and Queckenstedt s test is positive If the tumour is in the cervical region as is unusual all the foregoing changes are less intense

Radiographic examination may reveal an outline of the tumour at the level deter mined clinically or more often it shows some change in the shape of the pedicles of the vertebral arches or an increase of the interpeduncular distance Myodil introduced into the theca is held up and its border in contact with the obstruction displays the outlines of the surface of the tumour

Diagnosis—With such manifestations the diagnosis of meningioma is most prob able, but the diagnosis from other forms of intrathecal obstruction is not certain until the tumour is seen at operation The diagnosis from extra thecal compression is usually easier With spinal caries root pains are rarely so severe signs of bone disease are rarely absent and the paralysis is usually bilateral from the beginning and is severe by the time sensory loss develops The distinction from vertebral new growth is generally made or confirmed by radiographic examination but may for a time be impossible when bone symptoms and radiographic signs are absent

Course and Prognosis—The growth is often extremely slow Root symptoms may precede paralysis by months or even years and the weakness may increase gradually for several years before walking becomes impossible In the absence of operation it progresses eventually to complete motor sensory and sphincter paralysis possibly with paraplegia in flexion Most patients with simple tumours come to operation during the second year after the onset of the first symptom The prog nosis for recovery of power after removal of the tumour depends in part on the duration of the weakness in the lower limbs Complete recovery may be expected if it has not lasted more than a year and if sphincter control has not been lost Re covery from severe paralysis takes from 5 to 9 months When the paralysis is of longer duration recovery though gratifying is rarely complete Nevertheless full return of power has been seen after 3 years of severe paralysis

Treatment—This is obviously surgical The mortality after operation for the removal of simple tumours is low in skilled hands During the recovery stage follow ing removal of the tumour the treatment after the operation wound has healed is that of spastic paraplegia in general (p 1533)

NEUROFIBROMATA

Ætiology and Pathology—Neurofibromata within the spinal theca affect both sexes and occur mostly in early middle life They arise on the spinal nerve roots and may be solitary or multiple In cases of neurofibromatosis the occurrence of small neurofibromata on many of the lower spinal roots is the rule although they

as in other forms of tuberculosis The general condition of the patient is to be improved by fresh air, a liberal diet, cod liver oil and iron and great care is to be taken to prevent bed sores cystitis and deformities of the limbs Laminectomy is in general contraindicated and operative intervention of any kind should only be undertaken by a surgeon who has special experience of this disease After the bony disease has healed fixation of the spine by Allbee s operation or a modification thereof is called for in a few cases

TUMOURS OF THE VERTEBRAL COLUMN

Vertebral tumours are about twice as common as all the other forms of extra medullary tumours together and almost all of them are malignant Carcinoma is always secondary and is a frequent and distressing complication of cancer elsewhere A very small primary carcinoma *e g* of the breast lung thyroid or prostate may produce extensive disease of the vertebræ Evidence of compression may appear before the existence of the primary growth is suspected but on the other hand such may occur several years after complete removal of the primary growth and may even be the first evidence of a recurrence Sarcoma though the commonest form of primary growth is relatively rare and it begins in the bone or periosteum of the bodies or laminæ Primary sarcomata are sometimes multiple Secondary sarcoma arises by metastasis from sarcoma elsewhere or by direct extension from a growth in neighbouring soft parts *e g* of tumours in the mediastinal and retroperitoneal spaces

The growth of vertebral tumours is usually rapid and extensive portions of the spinal column may be completely destroyed The cord is compressed by the growth itself by displaced bone or by a process of the growth which invades the spinal canal through an intervertebral foramen As a rule the dura mater sets bounds to its inward extension Benign tumours of the spine are rare They usually grow forwards but occasionally an osteoma or an exostosis produces signs of compression

Symptoms —In most cases these are typical of spinal compression Root pains are usually severe and may be agonising but occasionally they are absent Not infrequently the onset of paraplegia is rapid paralysis developing in the course of 24 or 48 hours No deformity of the spine is ordinarily apparent but local tenderness is usual and radiographic examination reveals bony disease at a level corresponding to it Lumbar puncture reveals the signs of thecal obstruction

Diagnosis —When root pains occur in a patient with malignant disease or from whom a malignant growth has been removed the diagnosis of secondary growth in the vertebral column is most probable even though radiographic examination fails at first to reveal any deposits in the vertebral bones When pains are the first symptom mistakes are easily made because their root origin is not recognised Diminished sensibility in the painful area indicates the nature of the pain and this directs attention to the spine where tenderness or deformity is discovered As most vertebral tumours are secondary the next step is to examine the parts where carcinoma is common remembering that a small primary growth *e g* in the breast lung thyroid or prostate may give rise to widespread metastases in the bones In the absence of a history or signs of new growth in other parts the diagnosis is founded on the combination of local tenderness or deformity and rigidity of the spine with root or cord symptoms The severity of the root pains and their great aggravation by movement are characteristic

Course and Prognosis —When sarcoma or carcinoma spreads to the vertebræ from surrounding parts the duration of the disease is measured in weeks or months and death is due to the primary condition In primary sarcoma and in some cases of carcinoma of the vertebræ life may be prolonged for a year or two, and death is due rather to complications of the cord disease—bed sores cystitis etc

on the two sides especially in the lower limbs This is however, no more than a rule of thumb and there are many exceptions to it As long as the compression is relatively slight, motor tracts are more affected than sensory and consequently with the more slowly progressive conditions, weakness and spasticity of the lower limbs may precede sensory disturbances by a long period

TUBERCULOUS DISEASE OF THE SPINE

Synonyms —Spinal Caries Pott's Disease

This disease is the most frequent cause of slow compression It occurs most often in children, but is common in adults, and may begin late in life Signs of injury to the cord develop in about 1 case in 20 and are usually preceded by obvious deformity of the spine, but in many cases they appear before disease of the bone is suspected Rarely paralysis comes on for the first time in an adult who has had a curvature since childhood

The cord may be damaged by direct pressure of displaced bone, but more commonly by an abscess beneath the periosteum of the diseased vertebræ In almost all cases the injury is indirect and results from œdema of the cord arising from interference with its blood supply by tuberculous granulation tissue which forms on the outer surface of the dura mater and fills the epidural space (pachymeningitis externa) The functions of the cord may be temporarily deranged for long periods by this œdema without permanent damage to the nervous tissues hence when the disease is cured the œdema subsides and the cord recovers In cases of greater severity necrosis of the nervous structures follows thrombosis of the vessels, or prolonged pressure causes atrophy of nerve roots and complete recovery is impossible

Diagnosis —When spastic paraplegia develops in a patient who is known to suffer from tuberculosis of the spine the cause is obvious but when it precedes the appearance of signs of bone disease the diagnosis is difficult In all cases of compression the spine should be examined repeatedly for deformity tenderness and limitation of movement If tenderness is found constantly in the same place and the nervous symptoms are compatible with disease of the underlying segments disease of the bones is almost certain In young persons disease of the spine is usually caries and in adults also caries is not uncommon but tumours of the spine and aneurysm should be excluded Severe root pains are rare in spinal caries but are the rule in vertebral new growth A radiograph will usually demonstrate the presence and nature of the bone disease

Course and Prognosis —The course of the bone *disease does not always run* parallel with the paralysis and either may alter in severity independently but if the caries undergoes cure the paralysis usually diminishes Considering the severity of the paralysis the prognosis is favourable and astonishing recoveries occur *The outlook is best in young people with disease in the dorsal region* Many recover completely but more often especially in adults recovery though considerable is imperfect So long as the lower limbs remain spastic in the extended position together with exaggerated tendon reflexes the prognosis for complete recovery of power is good but if the limbs become flexed if they become flaccid if the knee and ankle jerks are lost if sensory loss is severe or if there is wasting in the limbs following damage to lower motor neurones, the outlook is bad Some patients live for years with severe paralysis but life is constantly endangered by sepsis from bed sores ascending infections of the urinary tract, chest complications and tuberculous disease in other parts

Treatment —This is to be directed towards curing the bone disease in the hope that cure of the paralysis will follow and it usually does so Complete rest on the back and fixation of the spine for many months is the routine treatment and recovery commonly takes about 2 years Streptomycin and isoniazid *should be administered*

cord is usually lacerated and its fibres are torn and its circulation interfered with so that compression if present at all plays little part in causing the persisting symptoms and its relief brings about no amelioration Dislocation of the axis however provides possible exceptions to this rule Transverse lesions of the cord may also result from gunshot wounds Secondly disruption of fibres and laceration of other elements and minute hæmorrhages occur within a localised extent of the cervical cord as a result of acute flexion of the neck The damage is probably the result of the sudden traction exerted on the cord as flexion of the neck causes the cord to be pulled up wards When the muscles of the neck are relaxed a very moderate degree of violence may cause the head to fall forward producing sudden flexion of the neck and damage to the cord With greater violence there may be accompanying dislocation or fracture of the cervical vertebræ but in the typical case the spinal cord is not compressed Sudden extension of the neck as in diving accidents also may cause severe injury of the cord with or without vertebral dislocation or fracture

Fracture dislocation of the vertebral column is most common in the region of the fifth and sixth cervical vertebræ and in the lower dorsal region Crush fractures of vertebral bodies due to force transmitted longitudinally as when a patient falls from a height and lands on his feet usually affect the first lumbar or one of the adjacent vertebræ and the corresponding lumbar spinal roots or the roots of the cauda equina may be damaged The roots being peripheral nerves are generally believed to have greater power of recovery than the structures within the cord itself

Fractures of the vertebral arches pedicles or spines may be caused particularly by gunshot wounds and in association with them the spinal cord may be injured in greater or less degree

Symptoms —A sudden transverse lesion of the spinal cord gives rise at first to a condition of spinal shock in which most of the automatic functions of that part of the cord below the level of the lesion are temporarily abolished If this occurs at a high level death is usually immediate but if not flaccid paralysis of all four limbs results If the lesion is in the dorsal region the immediate result is a state of acute flaccid paraplegia with retention of urine due to flaccid paralysis of the bladder wall (detrusor urinæ) in severe cases all the tendon reflexes and the plantar and abdominal reflexes are at first absent and there is complete loss of sensory apprecia tion below the level of the lesion In some cases the degree of spinal shock is less and the abolition of spinal function is partial

With the traction injuries of the cervical cord there is seldom the same degree of spinal shock but temporary paralysis may be considerable sensory loss is usually partial and some or all of the reflexes are preserved Retention of urine is in most instances a matter of a few hours Paralysis of the hands with relative sparing of the upper arms is not infrequent in these cases As the fifth cervical segment is often involved in the lesion the supinator jerk which depends on this segment is often abolished but the flexion reflexes remain and tapping of the supinator tendon pro duces reflex flexion of the fingers This is called inversion of the supinator reflex The fibres of the cervical sympathetic (as they descend in the cord to emerge with the first dorsal root) are often involved in the lesion and in consequence there may be contraction of the pupil and a slight degree of ptosis of the upper eyelid on one or both sides At a later stage when the lower limbs have largely recovered wasting becomes apparent in the hands and forearms and the case presents a superficial resemblance to one of amyotrophic lateral sclerosis but the history of accident, the presence of sensory disturbances and such features as the absence of the supinator jerks and signs of disturbance of the sympathetic nervous system should help to make the distinction (see p 1556)

Course and Prognosis —In incomplete and mild cases as spinal shock passes off the reflexes begin to return Retention of urine persists for a variable time and if not prevented by catheterisation overflow incontinence ensues The Babinski reflex

Treatment—In many cases of malignant vertebral disease the clinical effects of compression are relieved by extension of the spine the patient being kept flat in bed with an underlying fracture board If the paraplegia improves a plaster spinal jacket can be applied and the patient may begin to get up again In favourable cases radiotherapy may then be considered When root pains lead to the discovery of a secondary deposit in the spine in a case in which the primary growth has been removed and there is no evidence of secondary growths elsewhere in the body, radiotherapy should be employed, paraplegia is prevented the pains are relieved and life is prolonged In slowly growing primary growths of the vertebræ laminectomy is indicated in order to relieve pressure or to prevent pain by cutting sensory roots or dividing the antero lateral columns of the spinal cord The operation is merely palliative but is often followed by considerable temporary recovery

PROTRUDING INTERVERTEBRAL DISK (CERVICAL AND DORSAL)

The protrusion of an intervertebral disk in the cervical or dorsal region is much less common than in the lower lumbar region The mechanism by which it occurs is the same at all levels as a result of trauma the cartilaginous annular portion of the disk is ruptured, and the semi solid nucleus pulposus is then gradually extruded In most cases the mass is protruded backwards into the vertebral canal, and causes compression of the theca In the cervical region the degree of compression of the cord which ensues is seldom severe

The clinical history of the case is that of spastic paraplegia coming on gradually some months after an accident Progress of the paraplegia is usually slow and after a time one arm or both arms may become spastic and may show a little muscular wasting At this stage the condition in most instances becomes stationary Sensory impairment is seldom demonstrable but there is usually a zone of hyperalgesia corresponding to the segment just above the level of the lesion Mild root pains across the shoulders are likely to be attributed to rheumatism In some cases however, root pains are the principal manifestation and may be ascribed to brachial neuritis

Unless there is a close association with a definite accident the diagnosis is always a matter of great difficulty and only occasionally can it be made with confidence The spinal theca in the cervical region is wide and the degree of obstruction is not sufficient to give a positive result with Queckenstedt s test After injection of Myodil the hold up is at best partial but in favourable cases a filling defect is revealed on the radiograph While the symptoms are progressing the differentiation from an intramedullary tumour of the cervical enlargement may be impossible, but the history of an accident, and the persistent absence of objective sensory loss should raise a strong suspicion of a disk lesion, and the eventual arrest of the progress excludes the presence of a tumour From disseminated sclerosis the diagnosis may be equally difficult but if it be recognised that all the manifestations are attributable to a single spinal lesion it is unjustifiable to postulate disseminated lesions and moreover many of the patients concerned are above the age at which disseminated sclerosis is likely to begin

Some of the cases have been relieved by surgical treatment and it is only by operation that the diagnosis can be established with certainty Failing operation the sufferers remain permanently disabled but a moderate degree of spontaneous improvement is not unknown Collars of different types are often prescribed to immobilise the neck and take some of the weight of the head off the cervical vertebræ but it is doubtful whether the effects obtained compensate for the inconvenience or discomfort

INJURIES OF THE SPINAL CORD

Ætiology—The spinal cord is a delicate structure Injuries of it occur in the first place in association with fractures and dislocations of the spinal column The

of the cord and in the meninges around it and some small vessels may be thrombosed but the lesion does not appear to be primarily thrombotic (see p 1469)

Symptoms —In the non syphilitic cases there may be malaise and a slightly raised temperature and sometimes pain of " root type at the level of the lesion for a few days before the onset of paralysis These symptoms are followed by weakness of one or both legs and paralysis may be complete from the waist down within 24 or 48 hours, in other cases it is complete in an hour or two in others though remaining incomplete, it may reach its full intensity in that time, while in still other cases, the onset is apoplectic *i e* the patient feeling some weakness sits down and within a few minutes is completely paraplegic.

In the syphilitic cases pain in the back frequently precedes the onset by several hours or a day or two

If the patient is seen soon after the onset he usually shows complete motor and sensory paralysis from the waist down with flaccidity of the muscles and loss of reflexes retention of urine is present and may have gone on to overflow incontinence If some power of voluntary movement or some sensation is preserved some of the reflexes usually persist too There may be from the first a zone of hyperæsthesia at the upper limit of the paralysis, and later a girdle sensation may develop at this site While the limbs are flaccid and sensation is absent bed sores may develop with great rapidity and in the paralysed bladder intense cystitis may occur The patient may die in the acute stage as the result of these complications More often sensation and the reflexes return after a few weeks and in course of time spasticity develops in the limbs with a variable amount of voluntary power There may be a partial Brown Séquard syndrome Remarkable recovery may occur in the course of many months but even then considerable disability usually persists In other cases there is no return of power and the bedridden patient succumbs in a few months to intercurrent disease

Diagnosis —The Wassermann reaction both in the blood and in the spinal fluid should always be done with the knowledge that the latter may give a negative result in syphilitic cases even when cellular increase is present Queckenstedt s test should also be done at the time of lumbar puncture in order to exclude conditions of thecal block Poliomyelitis is excluded by the presence of severe sensory loss It may not be possible to make the differential diagnosis from hæmorrhage into the sub stance of the cord but the latter is usually associated with more pain and after the first acute stage is over with a syringomyelic type of sensory loss Angioma of the cord usually gives rise to less acute paralysis coming on with less constitutional disturbance

Treatment —The treatment consists of good nursing with the most careful attention to the bladder After the constitutional disturbance of the early days has passed massage and passive movements should be given to the paralysed limbs

In the syphilitic cases a full anti syphilitic regime should be started as soon as possible (see pp 223 1458)

LOCAL VASCULAR LESIONS OF THE SPINAL CORD

Hæmorrhage into the spinal cord is uncommon apart from pre existing vascular abnormalities When it occurs it produces signs of an acute segmental lesion followed as a rule by those of more general hæmatomyelia (see p 1549)

Local arterial thrombosis is usually due to syphilitic arteritis

In old people who are the subjects of severe atheroma transient partial paraplegia occasionally occurs most of the symptoms passing off within 24 hours or less The mechanism of its causation is not fully understood

There is some reason to think that venous thrombosis in the cord may give rise

appears and is coupled after a time with withdrawal reflexes of the lower limbs Later the tendon reflexes return and a variable degree of sensory and motor recovery may take place In severe cases this does not happen and the condition remains one of complete physiological interruption of the cord at the site of the lesion After an interval the lower limbs may become the seat of frequent flexor spasms, and a state of paraplegia in flexion may follow Any stimulus applied below the level of the lesion may then give rise to violent flexion spasms in the legs contraction of the abdominal wall and extrusion of urine from the bladder—the mass reflex" of Head and Riddoch In the great majority of those cases in which the cord is completely divided, the paralysed muscles remain entirely inert and the only evidence of reflex activity is the development of automatic function of the bladder

In severe cases the outlook is always extremely grave With high cervical lesions, death, if not immediate, may occur within a few hours from respiratory paralysis With lesions at lower levels death is liable to take place within a few weeks or months from bed sores or infection of the urinary tract The cases of less severe injuries of the cervical spine usually make good recoveries Wasting and weakness may be left in the hands, and sensory disturbances particularly of a subjective nature may persist and affect one side of the body or both sides

Treatment—Cervical dislocation should be reduced under general anæsthesia and subsequently a plaster collar should be applied to the neck in order to prevent undue mobility until the damaged ligaments have healed In cases of cervical fracture a collar should also be applied because further displacement may occur during sleep or under other conditions of muscular relaxation

In cases of fracture of the spinal column with injury of the cord open operation is usually contraindicated Fracture of the vertebral arches on the other hand may call for operation and the removal of bony fragments from the spinal canal Pressure on spinal roots is usually relieved by the Watson Jones method of treating spinal fractures

The further treatment of injuries of the spinal cord is that of acute paraplegia (see p 1533) and in no condition is the most careful nursing and skilled medical supervision more urgently called for In general the retention of urine is best treated by immediate supra pubic cystotomy but if the nursing conditions are ideal and there is good prospect of recovery tidal drainage through an indwelling catheter may be preferable The bowels are best controlled by regular enemata

ACUTE TRANSVERSE MYELITIS

Ætiology—The condition is rare during childhood and mostly occurs during the first half of adult life The sexes are affected equally In most cases the cause cannot be determined While a number are syphilitic syphilis has long ceased to be the most frequent cause

Pathology—The cord appears healthy except in a short portion of its length comprising one or two segments The lesion is most frequently situated in the lower half of the dorsal region, and at its site the cord shows intense signs of disease and may be wholly or partly diffluent In some microscopic sections of the affected segments no normal spinal tissue may be found and in others though elements are spared in an irregular fashion nearly every portion exhibits some pathological change The adjoining segments are affected in lesser degree and elsewhere the cord is healthy Unless all the elements are necrotic there is evidence of inflammatory reaction in the diseased portions There is no evidence of primary arterial or venous thrombosis but intense congestion of vessels and minute points of hæmorrhage may be present In the syphilitic cases there is intense cellular infiltration within the affected portion

OTHER DISEASES OF THE SPINAL CORD

SYRINGOMYELIA

Synonym —Status Dysraphicus

Definition —A chronic disease characterised by the formation in the spinal cord and brain stem of long cavities with surrounding gliosis To the disease in the brain stem the term syringobulbia is often applied

Ætiology —In most cases the disease begins to cause symptoms during the period of growth and it is rare for their appearance to be delayed beyond the age of 30 Both sexes may be affected and males are more prone to suffer than females There is considerable indirect evidence that the disease depends upon a congenital abnormality and other somatic abnormalities may be present in the same patient Cavitation in the spinal cord may also occur in association with intramedullary tumours with spinal vascular disease with pachymeningitis cervicalis and with hæmangiomata of the spinal cord

Pathology —At necropsy the cord is enlarged and cross section reveals a cavity filled with clear or yellowish fluid It extends up and down for many segments and the lower cervical and upper thoracic segments are the most frequently and the most severely affected The cavitation is most marked in the posterior half of the cord and appears to arise at the base of one of the posterior horns or in the middle line behind the central canal The cavity does not represent a dilated central canal for this can often be found separate from it, though the two usually communicate More than one cavity may be present It is surrounded by glial tissue which is relatively acellular and often peculiarly translucent The blood vessels frequently show degenerative changes and the fluid within the cavity may give evidence of old or recent hæmorrhage The cavity is so placed that it interrupts the crossing neurones which convey pain and temperature sensations As it enlarges the anterior horns of grey matter become involved in its surrounding gliosis and the cells degenerate Ascending and descending tracts are affected either by pressure as a result of distension of the cavity with fluid or by the glial process The posterior columns always survive longest

In the medulla the disease affects particularly the floor of the fourth ventricle in the region of the hypoglossal nucleus and tends to extend as a slit antero laterally to a position just anterior to the descending nucleus of the trigeminal nerve In its course it may destroy the motor nucleus of the vagus and glosso pharyngeal nerves or emerging fibres of these nerves The slit interrupts (1) the internal arcuate fibres passing from the cuneate and gracile nuclei to the mesial fillet and (2) the fibres from the descending nucleus of the vestibular nerve to the posterior longitudinal bundle The development of this lesion thus (1) renders complete sensory loss which was previously of the typical dissociated type and (2) causes or increases nystagmus If the slit reaches far enough it also interrupts some or all of the fibres passing from the descending trigeminal nucleus to the fillet of the opposite side and so (3) causes dissociated sensory loss on the face on the side of the lesion The disease may extend up into the pons and in rare instances higher

Symptoms —*Disturbances of sensibility* —By far the most constant and characteristic feature of syringomyelia is a sensory loss of a peculiar kind which was named by Charcot the dissociated sensory loss This is a loss of sensibility to painful impressions and to thermal stimuli while sensibility to touch to vibration to position to passive movement and to the appreciation of location upon the skin remain relatively or entirely intact In other words those forms of sensibility which travel by a path crossing in the commissures of the spinal cord are lost because the lesion of syringomyelia destroys especially the region of the commissures while these

to local lesions involving a greater or less degree of paraplegia and the residual paraplegia following local extrathecal infective conditions has been attributed to this cause

Vascular abnormalities resulting from congenital malformation of blood vessels are not very uncommon in the spinal cord The most usual type is a racemose venous angioma situated partly within the cord and partly on its posterior surface These lesions are almost always in the lower half of the cord Pain of root type affecting the lower limbs and recurring in acute episodes is a salient clinical feature It may be followed or even preceded, by wasting and weakness of one or both legs and sphincter disturbance is usually present during the acute episodes The reflex findings are often anomalous

The diagnosis is seldom made until the angioma is exposed at operation

The superficial vessels should on no account be interfered with and surgical intervention must be limited to such symptomatic measures as dividing a posterior nerve root for the relief of pain

SPINA BIFIDA

The most common developmental abnormality of the spinal cord results from a failure of the neural tube to close perfectly and to separate completely from the surface ectoderm In consequence of the failure of separation the mesodermal tissues in which the vertebral arches develop cannot close over the posterior surface of the developing cord at the affected site, and spina bifida ensues Spina bifida is thus usually associated with some abnormality in the cord itself, and its significance as a clinical finding is that it is a pointer to a local fault of development in the cord

Spina bifida is not uncommon and in 90 per cent of cases affects the lumbo sacral region and in about 5 per cent the lower cervical region There may or may not be some abnormality of the skin over the affected vertebral arches or there may be a frank meningocele Hydrocephalus may be associated Severe degrees of malformation of the spinal cord are incompatible with life

Symptoms —Weakness of the lower limbs may be present from birth or from an early age and may increase or it may be first complained of about puberty when the vertebral column elongates and the spinal cord which in these cases is often adherent at its lower end becomes pulled upon The ankle jerks and possibly also the knee jerks may be absent and the muscles of the legs poorly developed and the feet hollow Congenital talipes may be present Control over the sphincters of bladder and anus is often imperfect the former being the more frequently and con spicuously affected Trophic changes may occur on the feet and there may be areas of anæsthesia on the feet and on the buttocks *Sometimes the sensory loss is of a* dissociated type

Diagnosis —If the symptoms have been present in some degree since childhood the diagnosis is usually easy and is confirmed by radiographic examination When symptoms appear at puberty or later and there is no external abnormality spina bifida may not be thought of but if tumour is suspected radiographic investigation is likely to be undertaken and a bony abnormality is revealed which is in keeping with the clinical findings

Prognosis —In the less severe cases the symptoms become stationary and are consistent with a normal duration of life In the more severe cases which live beyond infancy the patients become bedridden and succumb at a relatively early age

Treatment —In most cases because of the malformation of the cord no im provement can be expected from operation Treatment should otherwise be symptom atic and enuresis should be treated with full doses of belladonna

paraplegia may result And again in very rare cases such pressure may lead to total avascularisation and total transverse lesion of the spinal cord with the appearance of a complete flaccid paraplegia with incontinence total sensory loss and absent deep reflexes

Sphincter trouble is usually absent or slight and occasional but in cases in which paraplegia is severe any degree may occur

The skin reflexes of the trunk are diminished or absent and the plantar reflexes are of the extensor type according to the degree of pyramidal involvement. Some degree of pes cavus is often present The knee jerks and ankle jerks are increased while the arm jerks even in the absence of muscular wasting are characteristically absent

Spinal curvature is present in many cases It consists essentially in a kyphosis or kypho scoliosis of the upper dorsal region with a compensating lordosis and lateral curve in the lumbar region The upper convexity is to the left because of the major use of the right hand It is dependent upon paralysis of the trunk muscles from involvement of the anterior horns in the upper dorsal region and in addition dys trophic changes in the bones may be factors in its production It is more marked the earlier it commences during the period of growth and in cases in which heavy manual occupation has been followed

Trophic and vasomotor disturbances —Thickening of the bones or a condition of osteoporosis and brittleness may be met with More often Charcot s arthropathy occurs It differs in no way from the similar condition in tabes dorsalis but being confined to the joints of the analgesic region it affects those of the upper extremity The most characteristic of the trophic changes consists in thickening of the sub cutaneous tissue and of the skin itself which is seen in the hands The fingers become thick and swollen and lose their natural outline the tips become blunted and the knuckle folds thick and coarse and vasomotor disturbance renders them unduly red or even blue They have been termed sausage like fingers and often stand out in contrast to the wasting of the intrinsic muscles of the hand A similar condition affecting the whole hand is common and was termed by Charcot the fleshy hand or main succulente The analgesic condition of the hands and the therman æsthesia present expose them unduly to injuries and since the injuries are likely to be unnoticed or disregarded septic infection arises easily and the results of injuries burns and whitlows are frequently seen giving rise to further deformity from scars or loss of the terminal phalanges

Considering that the efferent neurones of the cervical sympathetic system have their origin in the brain stem and their exit from the spinal cord in the upper dorsal segments thus traversing the whole of the region usually affected by the lesion of syringomyelia the frequency with which *paralysis of the cervical sympathetic* occurs is easily understood It may be complete or incomplete unilateral or bilateral and is recognised by smallness of the pupil narrowing of the palpebral aperture (sym pathetic ptosis) and a peculiar flatness of expression on the side of the face affected with decrease or loss of sweating These signs are much more obvious when unilateral than when bilateral, for in the absence of the contrast which a normal side of the face gives they are often overlooked when bilateral

Morvan s disease —This is a condition of great rarity in which a chronic peri pheral neuritis is combined with syringomyelia with consequent very severe effects upon the extremities There is absolute loss of all forms of sensibility in the hands and in some cases also in the feet together with atrophy of the intrinsic muscles The cause of this complication of syringomyelia is unknown

Diagnosis —Syringomyelia has to be differentiated in its early stages from those diseases which cause slowly progressive muscular atrophy in the upper extremities and in its later stages from other lesions of the central region of the spinal cord Those cases in which the lesions are chiefly in the ponto medullary region must be distinguished from other slowly oncoming lesions of the brain stem

forms of sensibility which travel by paths which are uncrossed in the spinal cord are not affected

The destruction of the commissures in the lower cervical and upper dorsal regions produces the dissociated sensory loss symmetrically over the thorax and upper extremities, the distribution varying with the extent of the lesion Only rarely does the symmetrical sensory loss extend below the thorax for the reason that the spinal lesion does not often extend below the mid dorsal region Occasionally the sensory loss varies in depth extent and symmetry of distribution according to the completeness, extent and symmetry of the lesion Thus in early and slight cases, the sensory disturbance may not amount to more than a relative loss of pain and temperature confined to the hands and ulnar borders of the forearms, while in an advanced case there is usually complete inability to appreciate painful and thermal stimuli over an area which would be covered by a sleeved jacket The area often extends later over the neck and the face Combinations of the "sleeved jacket" sensory loss with hemianalgesia and hemithermanæsthesia often occur in cases where both the spinal lesion and the medullary lesion are present The dissociated sensory loss makes its advent insidiously and is often unnoticed by the patient and discovered for the first time on medical examination Or it may appeal to the patient who on bathing finds that he appreciates heat and cold upon some parts of the skin and not on others Not infrequently he finds that he injures himself or burns himself without noticing it at the time

Subjective sensibility is not often affected, and for the most part syringomyelia may be described as a painless disease but there are very notable exceptions Sensations of heat and cold dull fixed pains lasting neuralgic pains and lightning pains resembling those of tabes may occur These pains are confined to the regions which are the seat of the other symptoms

Muscular atrophy —This is met with in considerably more than half the cases Though usually bilateral it is often not symmetrical and may be entirely confined to one side The intrinsic muscles of the hands and the muscles of the ulnar side of the forearms are first and most affected in the ordinary run of cases The atrophy is often here confined but it may extend up the arm though it is unusual for the whole upper limb to be affected Sometimes the shoulder muscles are first affected and again the scapulo thoracic and humero thoracic muscles may be early involved The upper intercostals and that section of the muscles which supports the spine supplied from the upper six dorsal segments suffer but the scalenes seem generally to escape The muscular atrophy is strictly limited and is apt to become complete in the muscles affected Fibrillation is not usually present The lesions of the medulla may involve the motor nuclei of the cranial nerves Wasting of the tongue on one or both sides is not uncommon and its discovery in a young subject should always arouse suspicions of the presence of syringomyelia Unilateral paralysis of the palate pharynx and all the muscles of the larynx upon the affected side may occur from involvement of the nucleus ambiguous Similarly but in much rarer cases atrophic paralysis of the face of the trigeminal muscles of the sternomastoid and trapezius may occur from unilateral involvement of the corresponding motor nuclei Nystagmus is almost a constant feature

Contractures resulting from the muscular atrophy are commonly seen in the hands and the deformity resulting tends towards the 'claw hand type but hardly reaches the degree seen in ulnar nerve paralysis and is often much modified by trophic and vasomotor changes and by the results of injuries and whitlows

Other motor symptoms —The lower extremities almost invariably escape so far as atrophy of muscles is concerned but usually present a slight spasticity with the signs of involvement of the crossed pyramidal tracts This does not often produce much disability In cases however where the lesions involve the lateral region of the cord either by direct extension or by the pressure of distended cavities severe spastic

paraplegia may result And again in very rare cases such pressure may lead to total avascularisation and total transverse lesion of the spinal cord with the appearance of a complete flaccid paraplegia with incontinence total sensory loss and absent deep reflexes

Sphincter trouble is usually absent or slight and occasional, but in cases in which paraplegia is severe any degree may occur

The skin reflexes of the trunk are diminished or absent and the plantar reflexes are of the extensor type according to the degree of pyramidal involvement. Some degree of pes cavus is often present The knee jerks and ankle jerks are increased while the arm jerks even in the absence of muscular wasting are characteristically absent

Spinal curvature is present in many cases It consists essentially in a kyphosis or kypho scoliosis of the upper dorsal region with a compensating lordosis and lateral curve in the lumbar region The upper convexity is to the left, because of the major use of the right hand It is dependent upon paralysis of the trunk muscles from involvement of the anterior horns in the upper dorsal region and in addition dys trophic changes in the bones may be factors in its production It is more marked the earlier it commences during the period of growth and in cases in which heavy manual occupation has been followed

Trophic and vasomotor disturbances —Thickening of the bones or a condition of osteoporosis and brittleness may be met with More often Charcot s arthropathy occurs It differs in no way from the similar condition in tabes dorsalis but being confined to the joints of the analgesic region it affects those of the upper extremity The most characteristic of the trophic changes consists in thickening of the sub cutaneous tissue and of the skin itself which is seen in the hands The fingers become thick and swollen and lose their natural outline the tips become blunted and the knuckle folds thick and coarse and vasomotor disturbance renders them unduly red or even blue They have been termed sausage like fingers and often stand out in contrast to the wasting of the intrinsic muscles of the hand A similar condition affecting the whole hand is common and was termed by Charcot the fleshy hand or main succulente The analgesic condition of the hands and the therman æsthesia present expose them unduly to injuries and since the injuries are likely to be unnoticed or disregarded septic infection arise easily and the results of injuries burns and whitlows are frequently seen giving rise to further deformity from scars or loss of the terminal phalanges

Considering that the efferent neurones of the cervical sympathetic system have their origin in the brain stem, and their exit from the spinal cord in the upper dorsal segments thus traversing the whole of the region usually affected by the lesion of syringomyelia the frequency with which *paralysis of the cervical sympathetic* occurs is easily understood It may be complete or incomplete unilateral or bilateral and is recognised by smallness of the pupil narrowing of the palpebral aperture (sym pathetic ptosis) and a peculiar flatness of expression on the side of the face affected with decrease or loss of sweating These signs are much more obvious when unilateral than when bilateral for in the absence of the contrast which a normal side of the face gives they are often overlooked when bilateral

Morvan s disease —This is a condition of great rarity in which a chronic peri pheral neuritis is combined with syringomyelia with consequent very severe effects upon the extremities There is absolute loss of all forms of sensibility in the hands and in some cases also in the feet together with atrophy of the intrinsic muscles The cause of this complication of syringomyelia is unknown

Diagnosis —Syringomyelia has to be differentiated in its early stages from those diseases which cause slowly progressive muscular atrophy in the upper extremities and in its later stages from other lesions of the central region of the spinal cord Those cases in which the lesions are chiefly in the ponto medullary region must be distinguished from other slowly oncoming lesions of the brain stem

The age of onset during the later years of childhood and the earlier years of adult life is *important* and during this period slowly developing paralysis with sensory loss and with or without muscular atrophy should always suggest the possibility of *syringomyelia* Other causes which may produce this system group and which may be confused with syringomyelia are local lesions of the brachial plexus and especially the lesion produced by the presence of cervical ribs root lesions lesions of the central grey matter of the spinal cord, especially central tumours of the spinal cord, and hæmatomyelia That the peculiar sensory changes of syringomyelia are usually the first signs of that disease is important, but this rule has many exceptions both as to the nature of the sensory changes and as to their time of appearance When sensory changes are not an early sign the diagnosis has to be made from such diseases as progressive muscular atrophy, peroneal atrophy and myotonia atrophica

Local lesions of the peripheral nerves produce signs which are confined to the distribution of the nerve involved the sensory loss is to all forms of sensibility, and the condition is ordinarily unilateral While these features are sufficient to distinguish such lesions from syringomyelia in nearly all cases, nevertheless in certain rare instances of syringomyelia the sensory loss and the muscular atrophy may be so narrowly confined to the distribution of the ulnar nerve as to cause close resemblance between the two conditions Any sensory loss over the trunk or signs outside the distribution of the peripheral nerve will if present, clearly divide the two conditions

Cervical ribs may produce slowly progressive atrophy of muscles pains and sensory loss very difficult to distinguish from those resulting from syringomyelia The diagnosis in these cases is beset with peculiar difficulties for so frequently do cervical ribs produce no nervous symptoms at all that their presence when demonstrated does not argue that they are the cause of the symptoms Again cervical ribs are among the commonest of the developmental peculiarities which are so frequently seen in the subjects of syringomyelia Slow muscular atrophy and slowly oncoming sensory loss and perhaps pain characterise both syringomyelia and cervical rib paralysis and the distribution may be unilateral or bilateral in either condition, but it is only when the manifestations are strictly confined to the upper extremities and neck that difficulty arises The slightest physical sign outside of this region at once turns the diagnosis in favour of syringomyelia and of these signs cervical sympathetic paralysis sensory loss on the trunk and alteration of the abdominal and plantar reflexes are the most important A very careful search must be made for any such signs and the patient observed over a considerable time before a certain diagnosis is made

Lesions of the central grey matter of the spinal cord may produce a symptom complex closely resembling that of syringomyelia Central tumours of the spinal cord when of slow growth are hardly distinguishable inasmuch as the lesion of syringomyelia is in reality a central tumour of the cord The majority of central tumours however are of more rapid development and speedily produce severe paraplegia

Progressive muscular atrophy in its early stages may cause difficulty in diagnosis since the muscular atrophy in syringomyelia may occasionally precede the appearance of any sensory loss or may be well marked when the sensory loss is slight In this connection widely distributed fibrillation is of great importance in indicating a diagnosis of progressive muscular atrophy particularly if it be seen in muscles not conspicuously wasted In peroneal atrophy the atrophy of the intrinsic hand muscles is always preceded by a more extensive atrophy of the muscles below the knee which are rarely atrophied in syringomyelia

Syringomyelia of the brain stem (syringobulbia) may be distinguished from other lesions of this region by its insidious onset and the special tendency to the involvement of the lateral region of the medulla so giving rise to a unilateral paralysis of palate pharynx and larynx with hemianalgesia and hemithermanæsthesia on part

of the face and even on the opposite half of the body Often some signs of cervical syringomyelia coexist but the medullary lesion may exist alone and it cannot be too prominently borne in mind that any very slowly progressive lesion of the brain-stem of insidious onset may be of the nature of syringomyelia

Course and Duration—The malady commencing insidiously progresses very slowly, and often ceases to progress for periods which may amount to many years The tendency to the destruction of life is not great, but when rapid extension of the physical signs and especially of paralysis and muscular atrophy of the upper extremities and respiratory muscles occurs the end is likely to come quickly Signs of great distension of the cavities such as pain and rigidity of the neck and also severe and increasing paraplegia with sensory loss of all forms of sensibility below the level of the lesion point to a rapidly fatal termination In rare instances acute exacerbations of the manifestations occur and are followed by partial remissions Such episodes are due to hæmorrhage into the syringomyelic cavity and when death has occurred in the course of one of them the cavity has been found filled with blood

It is not unusual to meet with well marked cases in which the signs develop and increase during late childhood and early adult life, and then remain more or less in a stationary condition allowing an occupation to be followed until well after middle life has been reached, but with the advent of the degenerative period of life from 45 years onwards, there is often a slow increase of the disability which puts an end to useful capacity The patients succumb to intercurrent disease, and few reach the age of 60 years

Prognosis—Recovery never occurs but arrest of the disease for long periods is frequent Those disabilities which are the result of pressure or distension may abate spontaneously or as the result of treatment and in arrested cases training may bring about lessening of the disability Increasing symptoms especially if the increase be rapid are always a cause for anxiety and increasing involvement of the respiratory muscles is the gravest of events

Treatment—In the vast majority of cases nothing can be done to retard the slow but relentless progress of the disease and treatment is therefore symptomatic. Radio therapy has been used and occasionally diminishes the spontaneous pains Rarely the presence of a dilated cystic cord may justify surgical operation and evacuation of the cyst.

HÆMATOMYELIA

Synonym—Spontaneous Hæmatomyelia

Ætiology and Pathology—Hæmatomyelia or hæmorrhage into the spinal cord sufficient to cause symptoms is a rare disease It appears to arise almost exclusively when there is some abnormality of the spinal vessels and in particular some variety of angioma excessively rarely it is associated with syphilitic disease of the spinal arteries and equally rarely with hæmophilia Hæmorrhage may occur into a syringo myelic cavity The hæmorrhage is nearly always centrally situated and shows a strong tendency to spread longitudinally and may extend over many segments

Males are affected far more often than females and the main incidence is in the first half of adult life

The clinical effects resulting from trauma of the cervical cord have in the past often been attributed to hæmatomyelia and may be due to this cause but it is now known that in the majority of such cases no significant hæmatomyelia is present

Symptoms—Prodromal symptoms may occur in the form of local weakness or transitory sensory disturbances In most cases the actual onset is sudden and the symptoms attain a considerable severity in the course of a few minutes but they may continue to increase for an hour or two

The *symptoms vary according to the site* and the extent of the extravasation In the majority of cases at first there is paraplegia with more or less complete motor and sensory paralysis up to the level of the lesion and usually with pain at the upper limit of the disturbance As the hæmorrhage extends longitudinally these manifesta tions are quickly followed by a syringomyelic type of sensory loss

Sometimes but not usually blood is found in the cerebrospinal fluid

Diagnosis —The diagnosis of primary hæmatomyelia rests upon the sudden onset, the rapid development of symptoms, which soon come to a standstill, and the physical signs of a central lesion of the spinal cord The distinction has to be made from acute myelitis Acute myelitis though rapid in onset rarely shows the sudden development of symptoms seen in hæmatomyelia, and the sensory loss which accompanies it is *not of the syringomyelic type* Prodromata often precede the onset in both conditions

Prognosis —Hæmorrhage in the cervical region may be rapidly fatal from respira tory paralysis In the non fatal cases a variable degree of recovery occurs and in many a syringomyelic type of dissociated sensory impairment ensues the intensity of the loss being usually less than in syringomyelia

Treatment —The general treatment is that of any severe spinal cord lesion with paraplegia Absolute rest is essential When there is evidence that a syphilitic lesion of the spinal arteries is in question the treatment is that of spinal syphilis Angioma and other malformations of the spinal vessels are not amenable to surgical intervention

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

Definition —A progressive disease associated with pernicious anæmia in which the white matter of the spinal cord degenerates the incidence of the lesions being particularly on the posterior and the lateral columns

Ætiology —It has now been determined that when subacute combined degenera tion occurs pernicious anæmia is always present in some degree but the degree of anæmia is extremely variable The spinal affection is evidently not the result of the anæmia but the spinal disease and the blood disease are both due to the absence of an essential factor now identified as cyanocobalamin (Vitamin B_{12}) both are associated *with complete gastric achylia*

As in the case of pernicious anæmia familial incidence has been recorded First met with in the third decade of life the malady in former times became increasingly frequent until a maximum incidence occurring in the sixth decade while cases com mencing in the seventh decade were not uncommon Owing to the earlier recognition and adequate treatment of pernicious anæmia the condition is becoming increasingly rare in this country

The cases seen are often atypical and may occur in patients with Addisonian anæmia in whom the treatment has been inadequate The sexes are equally affected

Pathology —The pathological and clinical features of the disease were estab lished in a classical paper by Russell Batten and Collier published in 1900 The essential lesion is degeneration of the myelin sheaths and subsequent degeneration of the axis cylinders in the posterior and lateral columns Similar degenerative changes are found in the peripheral nerves The myelin swells and later disintegrates This change first occurs in the lower dorsal region of the cord and is first seen in the centre of both posterior columns and soon afterwards in the centre of either lateral column as small areas of a darker and more translucent appearance than the normal white matter It is only at an early stage of the disease that the anatomical picture is strictly one of posterior and lateral degenerations for soon after spots of degeneration appear on either side of the anterior median fissure and in other parts of the antero lateral columns The degenerated areas increase in size centrifugally

coalesce with one another reach the surface of the cord and eventually involve the whole of the white matter of the cord as seen in transverse section with the exception of the narrow zone of short internuncial fibres which everywhere clothe the grey matter Occasionally the disease is confined to the posterior columns

From its starting point in the lower dorsal region the degeneration spreads upwards and downwards in the white columns of the spinal cord by means of the occurrence of small isolated spots of degeneration in the posterior lateral and antero lateral columns which increase in size and thus join the area previously degenerated The degeneration tends to extend upwards indefinitely and in severe and advanced cases has been found in the pyramidal tract as high as the internal capsule

The lesions of the white columns entail the usual secondary degeneration both ascending and descending but these occur late and are often much less obvious than might be expected from the severity of the local lesions The destruction of the axons by the local lesions also causes a series of retrograde changes in the corresponding nerve cells and tigrolysis vacuolation shrinking and neurophagy may be conspicuous especially in the cells of Clarke s column and in the cells of Betz which give origin to the pyramidal fibres There is never any inflammatory exudate and a peculiar feature is the absence in untreated cases of any glial proliferation

When degeneration in the peripheral nerves is severe the muscles are conspicuously wasted in the later stages and the muscle fibres show great diminution in size and poor striation There is not any considerable increase of the muscle nuclei and little or no fibrosis is found

The blood —Usually the blood shows a hyperchromic anæmia of varying severity the hæmoglobin ranges from 35 to 75 per cent the lower of these figures being common the colour index is above the normal and may be as high as 1 6 Macrocytosis is present Anisocytosis poikilocytosis and polychromasia are common Normoblasts are often numerous and megaloblasts may be found in numbers In a few instances anæmia has been absent throughout the hæmoglobin content and the cytology being normal this has occurred chiefly in cases which have run an acute and fatal course in a few months Sternal puncture shows a megaloblastic marrow A relative lymphocytosis is almost always present and may reach as much as 55 per cent This change occurs early and is helpful in the confirmation of the diagnosis of the nervous disease Achlorhydria is always present in the stomach even after the administration of histamine

A careful investigation of the blood changes at various stages of the disease and of the post mortem findings in a large series of cases has proved beyond any possible doubt that the blood changes in subacute combined degeneration are identical with those met with in the various stages of pernicious anæmia. The cerebrospinal fluid is normal

Symptoms —(1) *Nervous* —In a large majority of instances the symptoms appear insidiously and without any recognised exciting cause Sometimes the onset is more rapid and may be preceded by gastro intestinal symptoms or the patient may go to bed for a few days with an attack of influenza and on getting up again may be grossly unsteady

The first nervous symptom is usually numbness or tingling in the feet and if the patient is asked he will usually admit that he has a slight sensation of the same kind in the fingers Less often the sensation in the feet is one of swelling or coldness or as if walking on cotton wool and in a few cases unsteadiness in walking is at first the only complaint Very soon weakness in the legs is experienced and the numbness gradually spreads farther up and the patient begins to feel unsteady in walking

Examination at this time reveals a slight degree of weakness in movement of the toes or in dorsiflexion of the feet diminution or absence of the ankle jerk probably an extensor plantar reflex and a variable degree of sensory loss, the latter is usually

most marked for vibration and for sense of position in the toes and then for light touch There may be some tenderness of the feet or calves Romberg's sign is positive The superficial sensory loss is at first only over the feet then it spreads up to cover a 'sock' area and later has a 'stocking' distribution pain and temperature impairment meanwhile being added to it Loss of deep sensation however generally predominates, and unsteadiness may be very pronounced at a time when other signs are slight or absent At the stage we are referring to there are usually no objective disturbances in the upper limbs although intense numbness in the hands may be complained of

If the condition is allowed to progress, either the signs of peripheral nerve disease or those of spinal cord disease may predominate In the former case the knee jerks become diminished and the ankle jerks lost the muscles below the knees become paralysed and flaccid and eventually waste, deep sensory loss is severe and there is loss of all forms of superficial sensation over a 'stocking' area The paralysed muscles become very tender flexion spasms may set in and every movement is agonising In the upper limbs a variable degree of sensory loss may develop with astereognosis in the hands and loss of superficial sensation over a 'glove' area. The supinator jerks may be abolished but rarely the biceps and triceps jerks If the signs of spinal cord disease predominate the legs tend to become spastic, the knee jerks are exaggerated but the ankle jerks are usually weak and the plantar reflexes are strongly extensor Sensory loss is less marked as a rule than when the signs of peripheral disease predominate but deep sensation is always greatly impaired and as time goes on there is considerable loss of pain and temperature appreciation extending over the lower limbs and to a gradually higher level on the trunk In the arms the tendon jerks may be increased Except in advanced cases sphincter disturbances are slight

The cranial nerve functions are usually unaffected but optic atrophy is an important complication which occurs in a small percentage of cases and the visual disturbances due to it may be the first symptom Slight nystagmus is common

Mental changes occur in a small proportion of cases at a time when the degree of anæmia is not sufficient to account for them Apathy mild dementia and confusional psychosis with impaired memory and disorientation are the commonest types of disturbance

(2) *Anæmia* —Although anæmia is one of the most characteristic features of subacute combined degeneration since it is found in every case of long duration at some time or other and moreover it is sufficiently striking as at once to suggest the diagnosis in at least two thirds of all the patients when they first come under observation for nervous symptoms yet it may be absent throughout the course of the disease in a rapid case and its appearance may be delayed until several years after the disease of the nervous system is manifest The anæmia in almost every case is identical in every respect with pernicious anæmia Of those cases in which the blood picture is not typical nearly all show megalocytosis with a relative lymphocytosis and a high colour index as do early cases of pernicious anæmia and it may be said with certainty that the longer the patient survives the greater the likelihood of typical pernicious anæmia developing The spleen has been found to be enlarged in many cases and the marrow of the bones is typical of pernicious anæmia as may be also the iron reaction in the liver and the changes in the myocardium and other muscles As in pernicious anæmia the tongue is clean and glazed and this occurs so regularly that any appearance of furring of the tongue may justly be said to exclude the diagnosis of this disease a history of soreness of the tongue is obtained if enquired for in more than half the cases Fractional test meals show an absolute achlorhydria as in pernicious anæmia The colour of the skin is often peculiar and striking even when anæmia is not severe and is best described as 'biscuit coloured' A bright malar flush upon this yellowish biscuit coloured background gives a characteristic

and vivid facial aspect in the earlier stages of many of the cases The manifestations common to all anæmic states breathlessness headache cardiac and venous murmurs and œdema are commonly present but hæmorrhages are infrequent Syncopal attacks may occur Attacks of diarrhœa are common but on the other hand, constipation may be obstinate Irregular pyrexia is almost invariably present at some period in the course of the disease and this quite apart from fever producing complications such as cystitis and bed sores In the later stages progressive emaciation is constant and if life be prolonged it becomes extreme

Diagnosis—In the early stages of the disease when peripheral paræsthesiæ dominate the picture the condition has to be distinguished from peripheral neuritis and occasionally from peripheral arterial disease In the well developed stages of the disease its recognition presents no great difficulty Attention is quickly attracted by the conspicuous anæmia and biscuit coloured skin Following a period of slight paraplegia the steadily increasing paralysis of the lower extremities producing complete and lasting helplessness the characteristic distribution of the sensory loss the irregular pyrexia the anæmia and the relatively late onset of sphincter trouble serve to separate this disease from other forms of paraplegia The change from the spastic to the flaccid type of paraplegia with loss of the deep reflexes and persistence of the extensor response which occurs in some of the cases in the late stages, is highly characteristic

In the earliest stages and before the appearance of any definite evidence of organic spinal disease there may be such disability as to suggest hysterical paraplegia or ataxia and only the examination of the blood may expose the real disease When there is evidence of organic spinal disease it is especially from disseminated sclerosis spinal tumour tabes dorsalis and polyneuritis that the diagnosis has to be made The preponderance of peripheral subjective sensations and the anæmic appearance should always suggest a diagnosis of subacute combined degeneration Slight spastic ataxia is the common clinical picture of subacute combined degeneration of disseminated sclerosis and of spinal tumour The presence of objective peripheral sensory loss is in favour of subacute combined degeneration whereas diplopia nystagmus transient amblyopia and intention tremor are strongly in favour of disseminated sclerosis Spinal tumour is especially distinguished by a sharp line of sensory loss transverse to the axis of the body which does not spread up from below in slow fashion

When subacute combined degeneration commences with flaccid ataxia and loss of deep reflexes the distinction must be made from tabes dorsalis The extensor plantar reflex which is almost always present in the former disease and which is rare in early tabes the different distribution of the sensory loss in the two diseases the loss of power and associated anæmia in subacute combined degeneration and the results of the examination of the blood and cerebrospinal fluid for syphilitic reactions and of the latter fluid for lymphocytosis are important aids in the differential diagnosis

It is also necessary to bear in mind the strikingly close resemblance the disease we are considering may bear to polyneuritis The differentiation may in the early stages depend chiefly if not wholly upon the examination of the blood and the result of a fractional test meal But sooner or later the appearance of an extensor response will indicate the presence of a cord lesion On the other hand in the spastic type the presence of muscular tenderness in the legs is a strong indication in favour of subacute combined degeneration

Course and Prognosis—Before the days of effective treatment the duration of the disease varied within wide limits In some the progress was rapidly downhill survival being a matter of months from the first recognition of the symptoms in others the disease remained for several years in a relatively mild stage and partial remissions were common but once the patient became bedridden the survival period was usually short

With the advent of liver therapy for pernicious anæmia the outlook for subacute combined degeneration was not at first greatly changed but with more potent liver preparations and the development of an adequate technique of treatment, improvement and, later cure soon became apparent For the case that comes under intensive treatment before the patient has become quite unable to walk functional cure usually takes about 6 months to a year Some reflex abnormalities which mean nothing to the patient may still persist for a time or permanently Some authorities believe that cases of the flaccid type, in which the element of peripheral neuritis predominates, respond better to treatment than do those that are more spastic, the disease in the latter being chiefly in the spinal cord No such generalisation can however be made and in cases of the latter type the extensor plantar reflex usually the most persistent sign of spasticity may disappear Advanced cases of both types may fail to show much response to treatment But no case however advanced when first recognised, should be deprived of full treatment on this ground, and the most surprising recoveries are sometimes seen If treatment is stopped relapse occurs sooner or later, and with renewed treatment recovery again ensues but it is doubtful whether this process can be frequently repeated on account of the probability of gliosis in the spinal cord

Treatment —Whatever the degree of anæmia present intensive replacement treatment is essential Cyanocobalamin (Vitamin B_{12}) has now for practical purposes superseded the various forms of liver concentrates For the first month this should be given in doses of 100 microgrammes on alternate days Thereafter the dosage may be very gradually reduced provided that the blood picture is satisfactory and the ultimate maintenance dose may be as little as 100 microgrammes monthly The blood count should be brought up as quickly as possible to five and a half million red cells per cubic millimetre and kept at that level The more advanced the stage of the disease the more prolonged will need to be the period of intensive treatment and the more severe the residual disability is likely to be

Any suppurative condition of the body should be energetically treated Every care should be taken to prevent bed sores and cystitis When present these are often amenable to treatment in the early stages of the disease and also in less acute cases but in the later stages and in the more acute cases they are inevitable and the bodily vitality is too low for any reparative process to take place Pains are relieved by such analgesics as aspirin acetanilide amidopyrine and phenazone Flexor spasms are among the most troublesome of the symptoms since their frequent occurrence denies sleep to the patient and they are most important factors in the occurrence of bed sores The remedy which seems to have most effect in checking these spasms is barbitone

PROGRESSIVE MUSCULAR ATROPHY

Synonyms —Motor Neurone Disease Amyotrophic Lateral Sclerosis

Definition —It is usual to describe together a large group of cases in which progressive wasting of the musculature of the body and a moderate degree of spasticity are associated with and evidently secondary to widespread degenerative changes in the central nervous system the chief incidence of which is on the lower and upper motor neurones Clinically the cases are capable of great variety according to the sites of the initial wasting and the degree of spasticity but they are nearly all comprised by three clinical types In the first and most common type the wasting begins in the upper limbs and the lower limbs become spastic but do not waste This variety was called by Charcot *amyotrophic lateral sclerosis* In the second type the wasting commences in the muscles innervated from the medulla and pons and the names *progressive bulbar paralysis* and *labio glosso pharyngeal paralysis* are applied to it In the third type the wasting begins in or quickly spreads to the lower limbs and no

spasticity develops this is called the *purely atrophic type* Transitions between these types may be met with and the first two are frequently combined

Ætiology—The disease is rare before the age of 25 but occurs at all ages there after attaining its maximum incidence between 30 and 45 Males are affected much more frequently than females No causal factors have been discovered The patho logical findings are most in accord with the suggestion that the malady is due to a deficiency of some element essential to the nutrition of the spinal cord in the same sense that subacute combined degeneration and pellagra are the results of such deficiencies The question of the relation of trauma to the causation of progressive muscular atrophy admits of no decisive answer In occasional instances the onset follows more or less closely on an injury but we know of no pathological process whereby a peripheral injury can set up a diffuse degenerative process within the central nervous system Injury of the cervical portion of the spinal cord may produce a syndrome embracing wasting in the upper limbs and spasticity in the lower limbs (see p 1541) thus superficially resembling amyotrophic lateral sclerosis but there is not sufficient evidence that trauma can cause the progressive and ultimately fatal malady of which true amyotrophic lateral sclerosis is the most common clinical variety (see Diagnosis p 1560)

In rare instances progressive muscular atrophy has been described in the subjects of old acute anterior poliomyelitis Certain cases of syphilitic amyotrophy (see p 1470) present clinically a close resemblance to amyotrophic lateral sclerosis

Pathology—While in the less advanced cases the degenerative changes are almost limited to the anterior horn cells and the pyramidal tracts in the most advanced they affect almost all the structures of the cord with two striking exceptions namely the fibres of the posterior columns and the fine fibres passing forward in the grey matter It will be noted that the former fibres and probably the latter also have their cell bodies outside the central nervous system The latter probably subserve reflexes their preservation seems to be constant in amyotrophic lateral sclerosis and *not in other forms of progressive muscular atrophy and it is probably to be* correlated with the preservation of the tendon reflexes in the wasting muscles which is a peculiar and striking clinical feature of amyotrophic lateral sclerosis

To the naked eye a cross section of the spinal cord may show some diminution in size of the ventral horns The essential lesion is a primary degeneration of the cells in the ventral horns of the spinal cord and in the homologous motor nuclei of the brain stem namely the hypoglossal facial trigeminal and oculo motor nuclei Coupled with the degeneration of the lower motor neurones is a degeneration of the upper motor neurones of the pyramidal system In the ventral horn cells the degenera tion is evidenced by a gradual shrinking in size of the cells which lose their dendrites and become oval or spherical in shape The Nissl bodies slowly disappear and only in rare and rapid cases is definite chromatolysis seen The nuclei dwindle and become irregular and distorted

The dorsal and lateral horns are almost invariably intact but degenerative changes are sometimes seen in the cells of Clarke s column The affection of the motor nuclei of the brain stem in the bulbar cases is in every way similar to that of the ventral horns The degeneration of the motor nerves which take origin from the degenerate ventral horn cells often proceeds *pari passu* with the degeneration of the cells but in some cases this is conspicuously not so

The affected muscles are soft and toneless and the muscle fibres are found irregu larly degenerated bundles of normal and of degenerating fibres being found side by side until the atrophy is complete The characteristic change is shrinkage of the affected fibre to a calibre much less than normal As is usual in all slow tissue de- generations fibrosis and local arterial disease accompany the atrophy of the muscle fibres

The pyramidal neurones (cells of Betz) which characterise the precentral cortex undergo a degeneration very similar to that of the ventral horn cells but with this

difference that the earliest structural changes are found in the most distal part of the pyramidal fibres The degeneration of the upper motor neurones never proceeds to the complete destruction of anything like all the pyramidal fibres Degenerative changes are constantly present also in the anterior columns of the spinal cord

The pathological picture, therefore of progressive muscular atrophy is a widely scattered degeneration of nervous elements, not confined to the motor systems though these are predominantly affected

Symptoms—The onset is in most cases very gradual, but it may be more rapid and severe incapacity may result in the course of a few months In rarer cases, a severe degree of paralysis may develop in the course of a few days and in such cases it is not uncommon to see the most remarkable temporary improvement The nature of the onset as a rule, indicates the course which the malady will pursue A very slow onset is followed by a very slowly advancing disease often interrupted by long stationary periods whereas the more rapid the commencement the quicker will be the advance and the sooner will a fatal issue occur Accompanying and sometimes preceding the onset and not infrequently conspicuous during the early states of the disease, are certain sensory symptoms which from the confusion in diagnosis they may cause and from the scant attention which has been paid them in descriptions of the malady hitherto, deserve emphasis These symptoms are confined to the regions where the wasting first appears and consist in a subjective feeling of stiffness and uselessness much increased when the limb or the body is cold Or there may be dull aching pains intermittent neuralgic pains which may be severe or a sensation of coldness or numbness which may be intense Painful cramp in the muscles which are about to be affected is comparatively common The attention of the patient may be first drawn to his malady by the altered appearance produced by the atrophy, and this is more common when the commencement is in the hands where the subcutaneous tissue is thin and the region constantly in view More often the disability consequent upon the weakness is noticed first, this is always the case where the commencement is in the bulbar muscles and usually also where the muscles of the legs proximal muscles of the arms and trunk muscles are first involved Lastly the fibrillation may be so marked as first to attract notice

The *muscular wasting* which constitutes the most characteristic feature of the disease may commence in any group of the skeletal muscles whatsoever It may be first manifest in such rare situations as the facial muscles intercostal muscles muscles of the back and abdominal muscles The commonest situation is in the muscles of the upper limb where the distal (intrinsic muscles of the hand) or the proximal muscles (deltoids spinati etc) are first affected in about an equal number of cases In the hand the muscles of the thenar eminence are the first to waste and this is followed by atrophy of the hypothenars of the lumbricals and of the interossei with the usual flattening of the palm exposure of the flexor tendons in the palm from loss of the bulk of the lumbricals hollowing of the interosseal spaces and a tendency to the claw attitude of the hand This *main en griffe* is never so marked in this disease as in paralysis of the ulnar nerve syringomyelia etc because the wasting soon affects the long flexors of the fingers and moreover contractures of the affected muscles are not marked in progressive muscular atrophy When the upper arm is primarily affected the wasting is usually first seen in the deltoids whence it spreads upwards involving the spinati and the muscles attaching arm to scapula and arm and scapula to trunk Among these muscles some tend to escape the atrophy relatively or to be affected much later than others and these are the triceps the latissimus dorsi the lower half of the pectoralis major the levator anguli scapulæ and especially the upper half of the trapezius which for this reason was called ultimum moriens by Duchenne In the limbs the wasting always commences in one limb but soon spreads to the corresponding limb of the opposite side and tends ultimately to become symmetrical

The type of muscular wasting which is characteristic of amyotrophic lateral sclerosis and present less often in other forms of progressive muscular atrophy is that which was called by Gowers *tonic atrophy* It might be expected that when degeneration began in a group of anterior horn cells the corresponding muscles would gradually lose their tendon reflexes and become inexcitable But in amyotrophic lateral sclerosis while the muscles waste their tendon jerks become and remain exaggerated and the wasting muscles though they hang flabbily on the limbs become hyperexcitable to percussion and they show spontaneous contractions of groups of fibres known as fibrillary twitchings or *fibrillation* or fasciculation (see p 1559)

In other forms of progressive muscular atrophy the wasting muscles are more liable to lose their tendon jerks they may be inexcitable to percussion of the muscle bellies and they show less if any fibrillation

Accompanying the muscular wasting there is usually considerable wasting of the subcutaneous tissues and the skin becomes very loose and the reduced and separated muscles stand out when they are voluntarily contracted In some cases the subcutaneous tissue does not waste and may even be increased (especially in the lower limbs) and then the muscular wasting may be masked for a long time even till paralysis becomes complete There may be an appearance of vasomotor paralysis—redness blueness and some swelling of the periphery—but this seems to occur much more as the result of the continual pendent position of the hands and of the absence of muscular activity which normally aids the circulation than as the result of any definite vasomotor palsy

While in the most usual type of case muscular wasting is going on in the upper limbs slight signs of spasticity gradually develop in the lower limbs The knee jerks and ankle jerks become exaggerated and after a time the plantar reflexes become extensor There is not often a severe degree of spasticity and sometimes palpable spasticity is absent although the reflex signs of pyramidal disease are present The parts which become spastic do not in general develop any wasting

Spasticity from the upper motor neurone disease may develop in the lower extremities before there are any signs elsewhere of atrophic paralysis due to the lower motor neurone lesion and such cases present the physical signs of a primary lateral sclerosis It must therefore be borne in mind that a case presenting such features in an adult may eventually prove to be one of amyotrophic lateral sclerosis

In some cases of progressive muscular atrophy no abnormal clinical signs are found in the lower limbs but post mortem degeneration of the pyramidal tracts is evident

Next in order of frequency to initial wasting in the upper extremities comes the incidence of the disease upon the muscles concerned in facial expression articulation mastication and deglutition and in lesser degree upon the muscles of phonation The disease may be confined to these muscles throughout the whole of its course From the widely different clinical picture resulting and from the fact that all these muscles are supplied from the brain stem and upper two segments of the spinal cord this form of the disease has borne the name of *progressive bulbar paralysis* or *labio glosso pharyngeal paralysis* The wasting commences in the intrinsic muscles of the tongue and spreads thence to the orbicularis oris to the extrinsic muscles of the tongue pharynx and larynx to the muscles of mastication and eventually but in less degree to the facial muscles generally but only in rare cases are the oculomotor muscles affected

The intrinsic muscles of the palate the constrictors of the pharynx the intrinsic muscles of the larynx and the muscle of the œsophagus are little affected This seems at first an anomalous and astonishing fact, considering how great and important are the troubles with deglutition in bulbar paralysis But the anomaly disappears at once when one considers that the muscles which are concerned with buccal deglutition are

the muscles of the tongue, those forming the floor of the mouth including the mylo hyoid and the digastric, the muscles which raise and lower the jaw and those of the lips Further, the muscles which are most important in pharyngeal deglutition are those which raise and lower the hyoid bone and larynx as a whole, and these are the stylohyoid and stylopharyngeus, the palatoglossus and palatopharyngeus the genio hyoid, thyrohyoid sternohyoid, sternothyroid and omohyoid All these muscles are early and severely affected in bulbar paralysis, and when they fail, the intrinsic muscles of the palate are unable to shut off the naso pharynx, the constrictors of the pharynx are entirely unable to perform the act of deglutition and the intrinsic muscles of the larynx—though phonation is never lost—are unable since the larynx is unfixed by the extrinsic muscles, to modulate the tone of the voice The very active pharyngeal reflex and the difficulty in using the laryngoscope on account of spasm of the pharynx in the subjects of this disease are very good clinical evidence that the pharyngeal constrictors are not affected

The earliest physical sign of bulbar paralysis is the loss of the finer movements which are essential for correct articulation and consequently a slurring dysarthria develops and increases and the consonants become less and less distinct until they are inaudible The failure of the palate to close upon the posterior pharyngeal wall begets a nasal element in the voice Later the patient becomes unable to interrupt his blast at any of the stop positions and his utterance becomes a long moaning monotonous inarticulate sound His phonation remains, but he cannot alter its pitch nor divide it into parts of speech except by taking a fresh breath The orbicularis oris is early affected and the lips lose their firmness and become thin, and as they weaken the unopposed retractors of the angles produce a wide straight mouth both at rest and in emotional action Whistling and pursing up the lips become impossible and ultimately there is much dribbling of saliva for this can neither be retained by the lips nor swallowed The tongue shows fine fibrillation, and as it wastes it loses its point becomes rounded and is protruded with difficulty Its surface becomes dimpled and faceted in the end it consists solely of the covering mucous membrane the glands and the fibrous tissue and lies motionless in the floor of the mouth re sembling a crinkled mushroom The muscles of mastication all become affected The bite becomes feeble and the mouth cannot be opened against resistance In the late stages the jaw drops and the mouth is constantly open The combined weak ness of tongue and buccinators makes it very difficult for the patient to keep his food between his teeth in mastication and often he aids his disability by digital pressure upon the cheeks Nasal regurgitation is not uncommon The difficulty in swallow ing is greatest with fluids for these require quick action, and is next greatest with lumpy solids for these necessitate powerful action It is least with food of a porridge like consistency, and this should be carefully borne in mind in feeding the patients

The other muscles of the face are affected later and to a much less severe degree than is the orbicularis oris It is as if there were a physiological selection on the part of the disease for the nervous mechanism subserving mastication and deglutition Still in the majority of cases there is bilateral general facial weakness and wasting which with the peculiar mouth and dropping jaw produce a characteristic facies which can be instantly recognised If the upper facial muscles are tested by raising the eyelid with the finger against resistance invariably they will be found to be weak Only in very rare cases does the atrophy extend to the oculo motor muscles As in the paralysis of the limbs so also in bulbar paralysis concomitant signs of both upper motor neurone and of lower motor neurone lesion may exist When such tonic atrophy of the bulbar muscles is present the symptomatology and clinical appear ance are the same as have been above described for the simple atrophic form with the exception that the jaw jerk and the other muscle jerks of the bulbar region which are absent in the latter condition are brisk in the tonic atrophic form And

further it must be remembered that the additional element of spastic paralysis adds greatly to the degree of the paralysis as a whole

In less common cases of progressive bulbar paralysis the upper motor neurone lesion alone is in evidence and the bulbar paralysis is purely spastic Here the symptomatology as regards articulation deglutition etc is the same and the facial aspect identical with that of the simple atrophic and tonic atrophic forms The muscle jerks are brisk The appearance of the tongue however is quite different it is smooth narrow stiff and drawn into a narrow compass by the spasm of the muscles composing it It appears too small for so large a mouth There is no fibrillation and the muscles are nowhere wasted

The muscles of the back of the neck the splenius complexus etc., are not uncommonly the first muscles to be affected with the wasting of progressive muscular atrophy There is increasing difficulty in extending the head which drops forward causing a characteristic attitude which is associated with a constant overaction of the frontales which raise the brows to clear the line of vision when the head is dropped forward so giving rise to a permanently furrowed brow The loss of substance in the muscles of the back of the neck together with the dropping forward of the head causes the lower cervical and upper dorsal spines to stand out in undue prominence and to give an appearance approximating to that of an angular curvature

Primary affection of the lower extremities is much less common than that of the upper extremities bulbar region or neck muscles The anterior tibial and peroneal muscles are usually attacked first and less commonly the quadriceps The clinical type is that of flaccid atrophy in most of the cases Tonic atrophy which is so common in the upper limbs and in the bulbar region is rare in the legs

Wherever the site of commencement of progressive muscular atrophy may be it invariably spreads to other regions sometimes slowly and with periods of arrest which may last for years sometimes with remarkable rapidity The manner of spread is usually in terms of the contiguity of the affected elements in the nervous system but it is sometimes in terms of the physiological association of the muscles as is commonly seen in the bulbar forms of the malady When the disease is definitely installed the appearance of fibrillation in any muscles otherwise unaffected is a sure sign that atrophy will shortly commence in those muscles

According to the method of advance shown by the disease cases of progressive muscular atrophy fall into two groups which it is important to distinguish In the first group the atrophy spreads locally and slowly and remains confined to one region of the body during most of the course of the malady These cases are always of the simple atrophic type and they usually survive a long time Such cases however tend to become general just before the end In contrast with the local type of the affection is the group in which the manifestations commencing locally spread within a comparatively short time to many parts of the body or even become universal The spread may be very rapid and the end may occur in a few months or it may be slower but it is unusual for any of the cases forming this group to survive for more than 2 years This group comprises (1) the generalised cases of simple flaccid atrophy (2) all the cases of amyotrophic lateral sclerosis and (3) most of the bulbar cases

Fibrillation is a most important symptom of the disease and is an associate of the muscular atrophy It precedes the wasting of the fibres and is a sure herald of the advent of wasting in this disease It ceases to occur when the muscle is completely wasted and is not seen when the atrophy is not progressing On account of the importance of fibrillation as a diagnostic sign of progressive muscular atrophy it is important here to consider those other conditions in which it is met with clinically It occurs in syringomyelia and in peroneal atrophy but only when the muscular atrophy is progressing and therefore it is only an occasional symptom in either disease It is often very marked in cases of interstitial neuritis (sciatica etc) It

occurs in a most magnified and conspicuous form in certain conditions of gastro enteritis and is presumably due to an intoxication and to this form of fibrillation the term myokimia has been applied It is not met with in polyneuritis polio-myelitis, myopathy nor in the common gross lesions of nerve trunks nerve roots or spinal cord

The *electrical reactions* of the affected muscles vary according to the degree of degeneration Since normal and degenerate fibres are stimulated side by side in the affected muscle there will be *some lowering of the response to faradism with a* tendency to a polar change This is known as the ' mixed reaction and it is common to all diseases in which muscle degenerates fibre by fibre Faradic excitability lessens as more of the muscle fibres degenerate and when degeneration is complete all electrical excitability is lost In tonic atrophy the excitability of the affected muscles to direct mechanical stimuli such as percussion is increased so long as any living muscle remains

Contractures are conspicuous by their absence in this disease which is thus strongly contrasted with peroneal atrophy and some other muscular atrophies If the atrophy becomes complete in a whole limb the end result is that the limb is flail like and without contracture

Mental alterations are constantly present in the cases in which the bulbar region is affected Emotional instability and hyperexcitability are the usual change The patient is easily excited to tears or to laughter by trivial causes and when so excited cannot control his expression of emotion He himself feels little joy or grief during the paroxysms of laughing or crying

Sphincters —In the majority of the cases these are not affected but every now and then dysuria in any of its forms occurs and it may occur early in the course of the malady and it may be severe Loss of sexual power is very common

Reflexes —The reflexes are modified in this disease *on the one* hand by spasticity when this is present and on the other by the muscular atrophy which may prevent response in the affected muscles The pharyngeal reflex in bulbar cases is usually brisk, notwithstanding the statement to the contrary, which most writers upon this *subject have recorded but the response is not the normal response involving* all the muscles concerned in deglutition for these are atrophied and paralysed it is confined to the constrictors of the pharynx and the muscles of the palate with the feeble co operation of such of the somatic bulbar muscles as are still able to act *The plantar reflexes are usually of the extensor type when the legs are spastic* but this does not always obtain Similarly the abdominal reflexes do not disappear so constantly or so early as is the case in disseminated sclerosis for example and they may persist when the legs are markedly spastic and extensor plantar responses have appeared In cases of tonic atrophy the *tendon reflexes are everywhere increased* even in regions where the atrophy is severe and in this type of the malady they never disappear The same increase of the muscle jerks occurs in the purely spastic cases In simple atrophic cases the tendon jerks disappear *pari passu* with the wasting of the muscles

Cerebrospinal fluid —The cerebrospinal fluid is always quite normal by all the tests at present in vogue It does not usually contain more than one cell per c mm , and no change has been detected in its chemical constitution

Diagnosis —*The malady has to be distinguished from the many conditions* in which progressive weakness and wasting of the muscles occur from those in which muscular wasting and spasticity are conspicuous clinical features and lastly from other diseases in which bulbar symptoms are early evidenced Injury of the cervical enlargement of the spinal cord *gives rise to a limited degree of* wasting in the upper limbs and spasticity of greater or less intensity in *the lower limbs* (see p 1541) The wasting in the upper limbs becomes apparent some weeks after the injury and affects the muscles corresponding to the injured segments of the cord which are

commonly those of the forearms and hands But weakness of these muscles and the spastic weakness of the legs are maximal immediately after the injury, and power usually shows an improvement during the succeeding weeks or months whereas in progressive muscular atrophy the weakness wasting and spasticity come on insidiously and progress steadily It must be realised that although bony injury is commonly present injury of the cervical cord may occur without any fracture or dislocation of the cervical spine Furthermore a moderate degree of weakness of the limbs may escape observation while the patient is in bed after an accident, or they may be ascribed to other causes and so the signs resembling amyotrophic lateral sclerosis may not be discovered until several weeks after the occurrence of the lesion responsible for them Inversion of the supinator jerk (see p 1541) is a common sign in cases of injury of the cervical enlargement but rarely if ever occurs in progressive muscular atrophy Syphilitic amyotrophy (p 1470) may be indistinguishable from progressive muscular atrophy except by the results of the Wassermann reactions in the cerebro spinal fluid and blood Peroneal muscular atrophy very closely resembles progressive muscular atrophy in that slow wasting and fibrillation of the muscles are the chief clinical features The points which distinguish the two conditions are that peroneal atrophy is often a familial disease and is apt to commence in childhood when it is unusual for progressive muscular atrophy to begin The location of the atrophy is peculiar and when well marked in the periphery of all four limbs as is common in this disease cannot be confused with progressive muscular atrophy since the latter disease never has this distribution Syringomyelia is easily distinguishable by the early and striking loss of pain and temperature sensibility Cervical rib not uncom monly produces atrophy of the intrinsic muscles of the hand and though this is usually confined to one hand it may be bilateral Further it is exceptional for the atrophy to involve all the small hand muscles simultaneously or equally It picks out the opponens pollicis first and most severely and is not uniform for all the hand muscles as in progressive muscular atrophy Pain in the distribution of the eighth cervical and first dorsal roots and some loss of sensibility may be present. The atrophy remains local and is never accompanied by fibrillation The abnormal rib is easily discoverable on radiographic examination It must be borne in mind that cervical ribs are not uncommon and that their presence does not necessarily prove the cause of atrophy of the hand muscles for cervical ribs may be present in the subjects of progressive muscular atrophy syringomyelia or any other disease

The diagnosis of progressive muscular atrophy from the primary muscular dys trophies seldom causes serious difficulty The latter occur in general at a much earlier age and several members of a family may be affected the incidence of the wasting is almost invariably on the proximal muscles the weakness is out of pro portion to the apparent wasting fibrillation is absent and the progress of the disease is very much slower than that of progressive muscular atrophy Dystrophia myo tonica is at once separated from progressive muscular atrophy by the myotonus when this latter symptom is present When myotonus is absent, the characteristic wasting of the sternomastoids and of the muscles of the thighs the age of the subject and sometimes the presence of cataract should suggest the diagnosis Arthritic muscular atrophy occurs in the regions of joints which show easily recognisable disease Fibrillation does not occur nor are there alterations in the electrical excita bility of the wasted muscles

Lesions of peripheral nerve trunks may be diagnosed by the history of a local cause by the discovery of a palpable local lesion upon the course of the nerve and by the confinement of the atrophy to the distribution of one particular nerve while pain and sensory loss often occur in that same distribution

Lesions of the nerve roots and especially those produced by pachymeningitis and by neoplasm in the vertebræ may cause signs and symptoms so closely resembling those of the more rapid forms of progre sive muscular atrophy as to render correct

diagnosis very difficult Such a lesion in the cervical region for example may give rise to wasting of the hand and forearm muscles and a spastic condition of the legs resembling exactly a condition of amyotrophic lateral sclerosis, without deformity or rigidity of the spine and without pain or sensory loss In such cases of difficulty the course of a little time will bring the advent of the conclusive symptoms of a local pressure lesion It is important in this connection to remember that pressure upon the spinal cord results in hyperalbuminosis of the cerebrospinal fluid and if the lesion causing the pressure is syphilitic there is likely also to be lymphocytosis in that fluid neither of which conditions is found in progressive muscular atrophy

Diagnosis is most difficult in those cases where spasticity in the limbs is the first sign of progressive muscular atrophy and where such spasticity precedes the appearance of any muscular atrophy by a long time If it be clearly borne in mind that spastic paralysis may be the earliest and for a time the only sign of progressive muscular atrophy, and that among the many diseases of the nervous system which commence with the same clinical picture of spastic paralysis a certain diagnosis cannot be made until further distinguishing signs appear error will be avoided The importance of the examination of the cerebrospinal fluid in doubtful cases cannot be too strongly emphasised

Course and Prognosis —The nature of the disease is to progress and to extend its area of invasion until a fatal issue is reached The progress may be rapid and the end may be reached in a few months or it may be slow and several years may elapse before death occurs The local types of progressive muscular atrophy of slow onset are the most gradual in their development and these are often characterised by periods of arrest in the progress of the disease The generalised simple atrophic type of the disease is the most rapid especially when it commences with severe initial flaccid paralysis without atrophy

In the bulbar types of the disease, and in the common type of amyotrophic lateral sclerosis, the course is for the most, steadily progressive Every type will show how ever upon occasion exacerbations and remissions and the exacerbations are the most important and in the bulbar types may bring about the end in a few hours Of particular interest are rapid extensions of a flaccid paralysis which may occur in a few hours and which resemble and indeed are identical with onset of the disease with initial flaccid paralysis without atrophy, which has been already described Whatever type of the disease be present it tends in the end to spread and to become general

Involvement of the respiratory muscles or severe bulbar symptoms and the pulmonary complications which may accompany either condition, may bring about the fatal issue It is usual however for death to occur in a manner which is common to so many degenerative nervous diseases a rapid increase of the paralysis is associated with an increasing lethargy, which soon deepens into a rapidly fatal coma *It is* uncommon for death to occur from intercurrent maladies The average tenure of existence after definite signs are present is under 1 year in the generalised *flaccid* type and it may be as short as 2 months Bulbar symptoms are not generally survived for more than 12 months Localised cases of simple atrophy may *live for many* years Some of the patients in whom a positive Wassermann reaction is found improve and the disease is sometimes arrested by *antisyphilitic treatment*

The progressive character of the disease renders the prognosis grave in every case There are some cases occurring *in middle life which resemble* cases of progressive muscular atrophy of local distribution and slow course, which become finally arrested or even recover *the true nature of such cases* is doubtful but it is probable that they are allied to polyneuritis

In amyotrophic lateral sclerosis the average duration of life is seldom more than 3 years from the onset When bulbar symptoms are present the average duration is under 2 years In the generalised cases the average duration is under 1 year Widely

spread fibrillation in muscles which are neither weak nor wasted, is the constant herald of generalisation and renders the immediate prognosis serious In cases where syphilis is present the prognosis is more favourable and there is even a possibility of arrest and improvement if energetic treatment of the associated condition is provided Rapid extension of the weakness the advent of bulbar symptoms involvement of all the respiratory muscles and especially general asthenia and drowsiness are the signs which usher in the fatal result

Treatment —This malady seems to be entirely uninfluenced by any treatment that has hitherto been adopted At one time dramatic claims were made in respect of vitamin E (tocopherol acetate) given in doses of 3 mg thrice daily This was said to arrest wasting and weakness and in early cases to effect rapid improvement These claims however have proved illusory It remains therefore to secure favourable conditions of life for the patient and to maintain the general health in as perfect a state as possible Massage and passive movements are useful as giving bodily comfort to the patient and satisfying him that something is being done for him In bulbar cases the dysphagia must be aided by avoiding liquids and solids, and by serving all the articles of diet in pultaceous form Salivation which is so troublesome in this condition may be greatly helped by the administration of hyoscine or belladonna by the mouth

PERONEAL MUSCULAR ATROPHY

Synonyms —Charcot Marie-Tooth Type of Muscular Atrophy, Neuritic Type of Muscular Atrophy

Definition —This is an absolutely distinct and peculiar form of muscular atrophy, with a frequent tendency to occur in several members of the same family It usually commences in mid childhood and after progressing for some 20 years or less comes to a final arrest The atrophy always commences in the intrinsic muscles of the feet, and is throughout strictly distal in distribution The muscles of the face and trunk and the proximal muscles of the limbs are never affected The atrophy leaves a peculiar elastic fibrosis in the affected muscles so that the incapacity caused by this disease is much less than in any other form of muscular atrophy of like degree Sensibility is often slightly affected and there may be deep sensory loss The essential morbid anatomy is a primary neurone atrophy of the anterior horn cells and of some of the afferent neurones in Clarke s column

Ætiology —The disease usually commences between the fifth and tenth years of childhood but it may appear as late as the fourth decade of life Males and females are both affected Heredity plays an important part in the incidence although isolated sporadic cases are not uncommon It may exhibit every type of inheritance The malady often occurs in families and has been traced through five generations it may skip a generation and then reappear

Pathology —The anterior horn cells of the affected regions show a slowly progressive atrophy and disappearance with corresponding atrophy of fibres in the peripheral nerves The cells of Clarke s column show signs of degeneration as do also some of the fibres of the posterior columns of the spinal cord and especially those of the postero lateral column Slight degeneration in some of the fibres of the pyramidal tracts is usually found The affected muscles show a simple atrophy of the muscle fibres indistinguishable from that seen when a motor nerve is divided There is a simple shrinking of the fibres which stain progressively and more and more deeply with hæmatoxylin lose their striation and finally disappear Secondary fibrotic changes accompany the atrophy together with sclerosis of the arteries of the muscle

Symptoms —Muscular atrophy dominates the clinical picture of this malady

It is strictly distal in distribution and this feature will serve to distinguish peroneal atrophy from any other form of muscular atrophy This is to say it does not affect one particular muscle but the distal ends of all the muscles below a certain level on the limb leaving the proximal ends of the muscles normal and it advances up the limb inch by inch, the separation of the wasted portion of the muscle from the normal portion being always transverse to its length In other words, the muscle fibres seem to waste in terms of the length of the spinal axons which supply them The wasting commences always in the intrinsic muscles of the feet and hollowness of the instep and thinness of the feet together with retraction of the toes and the difficulty which the pes cavus so produced entails in fitting boots first draw attention to the disease As the process advances the lower segments of the anterior tibial peroneal and calf muscles become affected, and the limb is subsequently involved until the lower third of the thigh is reached, at which stage the disease is invariably arrested This slow spread of the atrophy from the distal towards the proximal portion of the limb, gives rise to a unique and characteristic feature in the appearance of the legs at the several stages of the disease As an example the complete atrophy of all the muscles below the middle and a well developed musculature in the upper half of the leg, give rise to the inverted fat bottle calf When the atrophy has involved the lower third of the thigh the lower end of the femur bare of muscle and covered only by skin and tendons contrasts strongly with the well developed muscles of the upper thigh and causes the thigh to resemble an inverted champagne bottle

Some years after the atrophy has become marked in the lower extremities and in the usual run of cases just before the age of puberty, the intrinsic muscles of the hands and first those of the thenar and hypothenar groups begin to waste and this wasting may extend as high as the middle of the forearm It must be borne in mind that the disease may become arrested at any period of its spread and especially that the upper extremities often escape altogether With the exception of the lower part of the thighs the proximal segments of the limbs do not become involved and the muscles of the head neck and trunk remain unaffected

The affected regions of the muscles waste absolutely, and leave a very elastic fibrous tissue The electrical excitability in the wasted regions becomes first lowered and then lost and in the earlier stages may show a mixed reaction in which there is lowering of excitability to faradism with a tendency to an inverted polar reaction Fibrillation of the muscles is an important sign It is seen only when the disease is progressing and in the muscles which are obviously wasting It is never general as in some cases of progressive muscular atrophy and since peroneal atrophy is at times advancing and at other times stationary, fibrillation may be in one case conspicuous and in another never seen It disappears entirely when the progress of the malady becomes finally arrested and is therefore useful as a clinical indication of active advance of the disease Contractures always occur and from the nature of the distribution of the atrophy are necessarily confined to the feet and the hands In the feet pes cavus with retracted toes is the rule but sometimes and in some stages of the disease the feet and toes may be dropped and the feet inverted The sphincters are unaffected The ankle jerks are diminished or lost in proportion to the wasting of the calf muscles In the final arrested stage they are usually lost The knee jerk is always retained and is usually brisk The plantar reflexes are usually lost early so far as any response in the foot is concerned but some response in the upper thigh muscles upon stimulating the plantar region often remains Pain tenderness and cramp are entirely absent. Conspicuous loss of sensibility is uncommon but slight loss of deep sensibility loss of the vibration sense and relative tactile loss may often be detected upon careful examination but in rarer cases all forms of sensibility may be severely affected or even entirely lost. Perforating ulcers may be met with upon the soles of the feet and are explained by the thinness of the feet and their deformity which coupled with the clumsiness of the use of the feet lead to the formation of

severe corns which break down into perforating ulcers Loss of sensibility also is a factor in their production

The most striking of all the clinical features of peroneal atrophy is the comparatively slight disability caused by the wasting of the muscles and consequent paralysis, and even the sensory loss when it is present

Course —The course is irregularly progressive for a number of years only and the advance of the disease ceases usually in the third decade of life Exacerbations of the weakness are likely to be followed in every case by considerable improvement, owing to the secondary fibrosis in the muscles

Diagnosis —Peroneal atrophy in the early stages is easily confused with progressive muscular atrophy in that wasting of muscles and fibrillation are the conspicuous features The onset usually in childhood and the fact that the feet are affected first the peculiar distal distribution and the presence of any familial incidence are important But the only distinction which is absolute is the distribution for progressive muscular atrophy may begin in childhood and peroneal atrophy may not appear till after middle life and often familial history is absent in the latter malady In the course of time the diagnosis always becomes clear for progressive muscular atrophy never keeps to the classic distribution of peroneal atrophy nor is it followed by the peculiar fibrosis which characterises the latter

Dystrophia myotonica when commencing in the peroneal muscles may for a time closely simulate peroneal atrophy The presence of the least sign of myotonia the involvement of the face and the atrophy of the sternomastoids will establish the diagnosis

The usual forms of myopathy are at once separated from peroneal atrophy by the distribution of the muscular weakness and wasting which in the former group of maladies is conspicuously upon the face trunk and proximal muscles of the limbs and in the latter upon the distal muscles Peripheral neuritis is more rapid in its onset and is apt to be associated with marked sensory disturbances both objective and subjective and the paralysis is in terms of individual muscles which is not the case in peroneal atrophy

Treatment —The general health should be carefully maintained and the nutrition of the affected muscles aided by the application of massage Care must be taken on the one hand to avoid over fatigue of the affected muscles and on the other to ensure such regular exercise as is compatible with their capacity Bicycling for example since it employs chiefly the thigh muscles is a better form of exercise for these patients than is walking In no circumstances should tenotomies be performed for the deformity of the feet for such measures tend to destroy the effect of the conservative fibrosis so essential to the production of a useful limb The use of heavy mechanical supports is to be avoided above all things Light well fitting boots so as to interfere as little as possible with the exercise of the damaged muscles are essential

PROGRESSIVE SPINAL MUSCULAR ATROPHY OF CHILDREN

Synonym —The Werdnig Hoffmann Disease

Definition —This is a malady of the first year of infancy often incident upon several children of the same parents and characterised by the gradual development of progressive muscular weakness and atrophy which affects the proximal muscles first and most increases to a complete paralysis of trunk and limbs and finally affects the bulbar muscles The disease is invariably fatal in from a few weeks to several months The most striking pathological changes are a progressive degeneration and disappearance of the ventral horn cells of the spinal cord and of their analogues in the brain stem

Ætiology —In some of the cases the paralysis is noticeable at the time of birth and the disease is obviously of pre natal development In others the children are quite healthy at birth, and the disease develops some time during the first year of life and most frequently within 8 weeks of birth Though sporadic cases may be met with, yet in the majority of instances several children of the same mother are affected Both the pre natal cases and the post natal cases may be met with among the children of the same mother The sexes seem to be equally affected No maternal ill health during pregnancy has been noticed, and nothing is known about any other ætiological factor

Pathology —The most extensive changes are found in the ventral horn cells throughout the spinal cord and brain stem and at many levels no normal cells what ever are to be seen Tigrolysis, swelling and glassiness of the cells extrusion of the nuclei disappearance of the dendrites shrinking of the cells and final disappearance is the sequence of the changes Degeneration of the anterior roots and of the peri pheral motor nerve fibres consequently occurs These changes are not confined to the lower motor neurones, for in some cases examination by the Marchi method shows extensive degeneration throughout the posterior columns of the cord indicating that lower sensory neurones were also considerably affected

The muscles show intense degeneration with hypertrophy of some fibres and atrophy of most of the fibres waving moniliform shape hypernucleation of the spindles, general nuclear increase and fibrosis

Symptoms —In the cases which are pre natal the malady is noticed at the time of birth on account of the tonelessness flaccidity and the poorness of movement in the trunk and proximal muscles of the limbs In the post natal cases there is a gradual onset of similar weakness and flaccidity in the trunk first and in the limbs afterwards which usually commences within 6 weeks of birth but which may not appear until towards the end of the first year of life The weakness seems always to be least marked in the periphery of the limbs where curious slow involuntary movements of the fingers and toes have been noted in many of the cases The paralysis is followed by a rapid and extensive wasting of the muscles, accompanied by occasional fibrillary twitchings Since these children are not only well nourished but often put on much fat during the illness wasting of the muscles may not be apparent on inspection or palpation It can however immediately be detected by radiography which distin guishes sharply between fat and muscle

As the malady progresses the trunk muscles become completely paralysed the intercostal muscles being always paralysed before the diaphragm The limbs become progressively weaker and lastly bulbar paralysis supervenes in those cases where death has not already occurred from respiratory paralysis The reaction of degenera tion is present in the affected muscles Sensibility may be unimpaired but in several of Collier s cases there was conspicuous loss of pain sensibility over the limbs and trunk The sphincters are unimpaired until the very last stages of the disease The superficial and deep reflexes are lost The ocular muscles are not affected and intelligence is preserved throughout

Diagnosis —The peculiar and striking features of the disease make the diagnosis easy if the symptomatology be known Amyotonia congenita presents the same helplessness and flaccidity of trunk and limbs as does the Werdnig Hoffmann disease and further resembles it in being sometimes congenital and sometimes having an onset very early in life In amyotonia congenita however the paralysis is not com plete, and it tends to improvement and not to progressive increase Contractures also occur which are not found in the Werdnig Hoffmann disease and, lastly the definite spinal cord changes of the latter malady are not found in the former Green field however considers that amyotonia congenita and Werdnig Hoffmann paralysis are different aspects of a single disease

Course and Prognosis —The course is invariably progressive and is more rapid

the earlier in life the disease commences and it is most rapid of all in the pre natal cases which are usually fatal within a few weeks With an onset some weeks after birth life is usually continued for several months and a few cases have been reported with an onset towards the end of the first year in which death has been delayed until the third or fourth year

Treatment —No treatment is known to influence the course of the malady

DISORDERS OF THE PERIPHERAL NERVES

LOCAL LESIONS OF NERVE ROOTS AND NERVE TRUNKS

Individual peripheral nerves may be damaged by a large number of agencies Trauma may affect them in a variety of ways Direct penetration by a sharp body such as a knife or glass or the passage of a fragment of a projectile may sever the nerve completely or partially Injury by a blow with a blunt agent or severe commotion in surrounding tissues such as occurs with the passage of a projectile near the nerve may destroy the axons without interrupting the continuity of the more resistant medullary sheaths and perineurium Recovery of such a nerve requires the growth of new axons down the surviving medullary sheaths Similar injuries of less intensity may temporarily abrogate the function of the nerve but be followed by recovery of function in a matter of hours or days For these three degrees of nerve injury Seddon has suggested the names neurotmesis axontmesis and neurapraxia respectively Nerves may also be injured by trauma of a less violent but more sustained character as is seen in the common varieties of pressure palsy such as Saturday night paralysis crutch palsy palsies from pressure of plaster and other splints and chronic over stretching as in the case of the ulnar nerve Peripheral nerve lesions may follow a variety of general infections such as pneumonia dysentery and streptococcal illnesses Nerves may be involved in specific inflammatory processes such as leprosy Finally they may be involved in new growths The most important example of this is in filtration with carcinoma from a neighbouring focus but nerves may be the site of isolated neurofibromata or multiple lesions in cases of Von Recklinghausen s neuro fibromatosis

PHRENIC NERVE

This nerve supplies the diaphragm Paralysis results most often from disease of the spinal cord but the roots may be implicated in disease of the spine and the trunk may be injured in its course through the neck and thorax by wounds or tumours Bilateral paralysis occurs in lesions of the cord and spine and in polyneuritis espec ially of the diphtheritic and acute infective varieties Other causes usually affect one side only When the diaphragm is completely paralysed the normal inspiratory protrusion of the upper part of the abdomen disappears or is replaced by retraction of this part with each inspiration During rest so long as the lungs are healthy the respiratory rate does not increase but if bronchitis or pneumonia arises as a com plication or if the patient exerts himself the diminished reserve of respiratory power is seriously felt When one nerve only is affected the diaphragm does not move on that side but becomes permanently elevated as a result of collapse of the base of the corresponding lung This is rarely detected by observation of the abdominal move ments but is easily seen on the radiograph screen It produces no discomfort

THE LONG THORACIC NERVE

This nerve supplies the serratus anterior muscle When all the fibres of this muscle contract the scapula moves upwards forwards and outwards It contracts

with the pectoralis major in the action of pushing forward the point of the shoulder and in the rapier thrust movement It also assists the deltoid in raising the arm When it is paralysed alone, the position of the scapula at rest is unaltered but if the trapezius and the rhomboids are paralysed as well the scapula drops and its lower angle is displaced inwards Paralysis of the serratus anterior is best demonstrated by causing the patient to hold the arms outstretched before him The arm is not raised so high on the affected as on the normal side, because the scapula is not fixed and the deltoid works at a disadvantage Viewed from behind the deformity is characteristic The vertebral border of the scapula stands out prominently and the hand can be pushed between this bone and the thorax— winged scapula On raising the arm from the side there is difficulty in attaining the horizontal position, but the winging of the scapula is less apparent

The nerve may be damaged by carrying heavy weights on the shoulder by falls or blows on the shoulder, and by continued muscular effort with the raised arm The nerve may be injured alone in gunshot wounds but as a rule it is associated with lesions of the brachial plexus In addition a serratus anterior palsy may develop suddenly in an otherwise healthy person after exposure to cold or as part of a rare reaction to the administration of serum or antitoxin In such neuritic cases and in the cases caused by compression severe neuralgic pains in the neck precede the onset of paralysis Recovery is always very slow and the defect may be permanent

BRACHIAL PLEXUS

The brachial plexus may be injured by stabs in the neck by penetrating missiles by dislocation of the shoulder or fracture of the clavicle or by pressure of a tumour aneurysm or cervical rib Further the nerves may be torn by forcible dragging on the arm in accidents or during delivery In most cases the lesion is partial and the symptoms conform in the main to one of the following types

Upper plexus paralysis (Erb s palsy) —This results from an injury to the fifth and sixth cervical roots The muscles paralysed are biceps deltoid brachialis brachioradialis (supinator longus) supraspinatus infraspinatus rhomboideus subscapularis clavicular portion of pectoralis major serratus anterior latissimus dorsi teres major The arm cannot be flexed at the elbow (flexors of forearm) nor raised and abducted (deltoid) The movements of the wrist and fingers are not impaired Adduction of the arm is weak (pectoralis major) and rotation is feeble or absent (spinati) On attempting to oppose the shoulders, the scapula on the affected side passes farther from the middle line (rhomboideus) The hand of the affected side cannot be placed on the buttock of the sound side (latissimus dorsi)

The reaction of degeneration is often complete in the deltoid and flexors of the forearm and nearly so in the spinati It is usually incomplete in the other muscles Sensation is diminished or lost along the outer border of the whole limb immediately after the injury but improvement sets in rapidly For some time the patient experiences pins and needles and burning sensations in the affected area which last longest in the thumb and index finger The biceps reflex is lost

Lower plexus paralysis (Klumpke s palsy) —This results from a lesion of the eighth cervical and first dorsal roots or of the common trunk of the median and ulnar nerves The intrinsic muscles of the hand and the flexors of the wrist and fingers are paralysed and the inner border of the forearm and hand is anæsthetic When the roots are damaged sympathetic fibres may be implicated with the production of myosis narrowing of the palpebral aperture enophthalmos and alterations in sweating on the face neck arm and upper part of the chest on the affected side

Middle plexus paralysis —This form of paralysis is a common result of gunshot injuries of the plexus It affects the muscles supplied by the radial and axillary nerves —posterior cord As the nerve to the latissimus dorsi arises from the same cord

this muscle is often paralysed as well In addition to these simple types more complicated paralyses occur in which various parts of the plexus are injured together

Paralysis of the medial cord of the plexus —Atrophy is confined to the intrinsic hand muscles and the sensory loss is confined to the hand

Incomplete lesions of the brachial plexus show a remarkable tendency to spontaneous recovery In many cases recovery is complete in 6 months to 2 years, in others it is partial and some muscles remain paralysed

THE RADIAL NERVE

Owing to its long course its position in relation to the humerus and its peculiar vulnerability to compression paralysis of the radial nerve is one of the commonest peripheral nerve palsies, although it is a mixed nerve containing sensory, motor and vasomotor fibres the symptoms of an injury are almost entirely motor In the upper arm the nerve supplies the triceps and the anconeus in the forearm the supinators the extensors of the wrist and fingers and the extensors and long abductor of the thumb

Injury to the nerve is followed by dropping of the wrist and fingers The wrist and the first phalanges are flexed The flexion is limp and easily reducible

When the lesion is in the axilla the whole of the *triceps* is paralysed and extension at the elbow is lost Occasionally in wounds of the posterior aspect of the arm the nerves to the triceps are injured whilst the main trunk escapes The patient is then able to extend the arm powerfully by means of the anconeus but if he is made to raise the elbow as high as possible with his fingers on the point of the shoulder extension of the bent forearm is impossible

In most cases the nerve is injured in the middle third of the arm and the triceps escapes but the brachio radialis and *all* the extensor muscles in the forearm are paralysed Partial paralyses such as are seen in lesions of the median and ulnar nerves are very rare The brachio radialis is not a supinator Its action is to flex the forearm whilst the hand is in a position intermediate between pronation and supination *Paralysis of this muscle is detected by the absence of contraction when* the pronated forearm is flexed against resistance Owing to paralysis of the *supinator* supination is abolished During the movement of flexion of the forearm the biceps acts as a supinator and during extension the external rotators of the shoulder correspond though feebly

Paralysis of the *extensors of the carpus* abolishes both extension and lateral movement at the wrist The flexors of the carpus play no part in lateral movements The *extensors of the fingers* extend the first phalanges *only* Extension at the distal joints is carried out by the lumbricals and interossei Paralysis of the *extensors and long abductor of the thumb* renders abduction of the thumb and extension of the phalanges impossible On attempting to abduct the thumb it passes no farther than the radial border of the hand In some cases the second phalanx of the thumb can be feebly extended by the muscles of the thenar eminence

Many muscles not supplied by the radial nerve work at a disadvantage when the extensors are paralysed These defects must not be mistaken for signs of injury to other nerves Owing to the flexed position of the hand the grasp is feeble but if the wrist is extended passively the grasp is improved The patient cannot make a fist properly as the thumb does not oppose the index finger and the fingers cannot be flexed into the palm until the thumb has been moved aside by the sound hand The movements of the interossei in abducting and adducting the fingers are also feeble while the wrist is flexed but are much stronger when the hand is resting flat on a table with the wrist and fingers extended The complete reaction of degeneration is often found in all the paralysed muscles from the onset Atrophy becomes obvious in a month or two It *extent and severity give important evidence for prognosis*

Sensory disturbances—Subjective symptoms are rare In a few cases, paræsthesiæ are felt on the posterior aspect of the forearm and on the dorsal aspect of the thumb They are of brief duration and are commoner with partial than with complete lesions Causalgia is almost never seen in lesions of this nerve Sensibility to light touch superficial pain and temperature is impaired over a small area on the radial border of the hand including the proximal joints of the thumb and the first two fingers The defect is often very slight, and is only discovered on very careful examination Deep sensibility is rarely affected Considering the extensive distribution of the superficial branch of the radial nerve it is rather surprising that the sensory disturbances are so slight when the nerve is injured above the origin of this branch

As a rule the brachio radialis recovers first then the extensors of the wrist then the extensors of the middle, ring little and index fingers in this order, and the extensors and abductors of the thumb last of all On palpation of the muscles during attempted extension contractions can be felt before any movement is produced Other signs of impending recovery are the disappearance of automatic pronation and of the flail like drop of the hand, also diminution of automatic flexion of the fingers after passive extension Recovery of movement is complete when the patient is able to extend the wrist and all the fingers simultaneously or separately After this becomes possible restoration of power is rapid

THE MEDIAN NERVE

Whilst the clinical individuality of the radial nerve is shown in the preponderance of motor symptoms and in the uniform completeness of the paralysis that follows an injury that of the median is seen in the frequency of partial and especially of painful lesions Isolated palsy of this nerve is infrequent except as a result of gunshot wounds and other injuries

Total Paralysis—The muscles paralysed are the pronators the radial flexor of the wrist the flexors of the fingers except the ulnar half of the deep flexor most of the muscles of the thenar eminence (opponens abductor brevis and outer head of the flexor brevis pollicis) and the two radial lumbricals Stated briefly the symptoms are inability to flex the phalanges of the index finger and the second phalanx of the thumb difficulty in flexing the phalanges of the middle finger, defective opposition of the thumb The appearance of the hand in total lesions is fairly constant The hand inclines to the ulnar side the index and middle fingers are more extended than is normal and the thumb lies on a level with the fingers—the ape hand

Pronation is incomplete and defective The patient tries to overcome the defect by rotating the whole limb at the shoulder Paralysis of the *flexors of the wrist* is seen when an attempt is made to flex against resistance The tendon of the ulnar flexor alone stands out and the hand is drawn towards the ulnar side Even at rest the flexor tendons are more prominent on the sound than on the affected side

Flexion of the fingers is good in the two ulnar fingers though weaker than normal The index cannot be flexed at all and the third finger only incompletely Flexion at the proximal joint is usually good in all the fingers including the index and flexion at this joint with extension at the last two joints is usually well done by the interossei and lumbricals If the proximal phalanx of the thumb is immobilised it will be seen that flexion of the terminal phalanx is abolished owing to paralysis of the *flexor longus pollicis*

Paralysis of the *thenar muscles* renders opposition and abduction of the thumb defective By means of the adductor the thumb can be drawn into the palm but as the radial fingers cannot be flexed nor the thumb opposed it is impossible to place the tip of the thumb on the tips of the fingers Atrophy of the muscles becomes obvious in a few weeks The outer part of the thenar eminence is flattened and the bulk of the muscles arising from the internal condyle is greatly diminished

Sensory disturbances —In almost every case there is complete anæsthesia to all forms of sensation in the two terminal phalanges of the index and middle fingers The skin outside this area may be unaffected even in complete lesions but in most cases sensibility is diminished in the terminal phalanx of the thumb and to a less extent over the remainder of the radial half of the palm including the radial side of the ring finger The stereognostic sense is lost in the outer fingers This defect together with the loss of power renders the thumb and index finger useless and makes paralysis of the median the most serious single nerve lesion of the upper limb

Vasomotor and trophic changes —In many cases the skin in the distribution of the median nerve is red dry and chapped and the nails white or purple and atrophy occurs in the pulp of the affected fingers

Recovery is slow and is rarely complete Sensation begins to return before power but the stereognostic sense is often defective long after movement in the fingers has returned The pronator and the flexors of the wrist recover first then the flexors of the thumb and middle finger Flexion of the index finger and opposition of the thumb if it is regained at all remains defective for several years In searching for signs of recovery, care must be taken lest some trick movement due to contractions of healthy muscles is misconstrued For example when told to flex the terminal phalanx of the thumb the patient first over extends and abducts and then relaxes suddenly The terminal phalanx then makes a slight passive movement of flexion which may be mistaken for true active flexion Recovery is complete when the patient is able to make a good fist with the fingers flexed well into the palm and the thumb pressed firmly upon the dorsal aspect of the second phalanx of the middle finger

PARTIAL LESIONS —Partial paralysis of the median nerve is much commoner than the complete form

Motor symptoms —Flexion of the index finger and opposition of the thumb are most impaired The flexors of the middle finger and of the terminal phalanx of the thumb may suffer also but to a less degree whilst the pronators and the flexors of the wrist often escape entirely

Sensory symptoms —Apart from the painful lesions to be mentioned later sensory troubles are usually slight in partial lesions Anæsthesia is rare but sensibility to all forms may be diminished in the areas mentioned under complete lesions

Vasomotor symptoms —The skin is often cyanosed in the distribution of the injured nerve and it may perspire more freely than in healthy parts These changes are more distinct when the paralysis is complicated by a vascular lesion

Recovery is naturally more rapid than in complete lesions The order in which the muscles recover and the tests for complete return of function have been mentioned above

PAINFUL LESIONS OF THE MEDIAN NERVE —*Causalgia* —In many cases the most prominent symptom of injury causing an incomplete lesion of the median nerve is *pain* It comes on about a month after the injury at first as tingling or pricking in the finger tips and palm later as a constant severe smarting dragging or *burning* pain—hence the name causalgia Added to the constant pain which never ceases day or night paroxysms occur in which the pain increases suddenly in intensity The application of cold water gives temporary relief and patients often wear bandages or gloves which they keep constantly moistened The pain is greatly aggravated by emotional influences

Vasomotor changes are a feature of this type In many cases perspiration is diminished over the radial half of the palm and the skin becomes dry and scaly In others perspiration is increased over the median area

Motor disturbances are always present but are usually slight the weakness affecting mainly the flexors of the index finger and the thenar muscles

In severe cases the limb is held flexed at the elbow and wrist with the hand

constantly raised and the fingers extended or hyper extended The whole hand atrophies and irreducible ankylosis occurs with the limb in this position The skin of the hand is thin and dry The fingers taper and the nails are long brittle blackened and striated longitudinally The pain reaches its acme 4 or 5 months after the injury and then slowly declines, but the limb remains useless Even in slighter cases without much deformity, recovery of function is extremely slow and is rarely complete The condition is often much improved by early operation and neurolysis of the nerve, or relief may be gained by sympathectomy

THE CARPAL TUNNEL SYNDROME —The median nerve may be compressed at the wrist as it passes through its tunnel in the transverse carpal ligament The condition is common in middle life in women engaged in housework laundrywork and other manual labour and also at an earlier age in women who have young children The chief complaint is of pain or numbness in the middle three fingers but frequently discomfort is complained of also in the forearm and this occurs particularly at night Pressure at the carpal tunnel is thus one of the causes of acroparæsthesia In the more severe cases wasting of the upper part of the thenar eminence may be observed and some sensory impairment may be found over the affected fingers At operation the median nerve is found compressed in its tunnel and swollen for a short distance proximal to its entry into the carpal ligament Opening up the tunnel relieves the symptoms In occasional cases some weakness of the fingers results in consequence of the failure of the weakened carpal ligament to retain the flexor tendons in their normal position

THE ULNAR NERVE

This nerve supplies the ulnar flexor of the wrist the ulnar half of the deep flexor of the fingers the muscles of the hypothenar eminence the interossei the two inner lumbricals and the adductor and inner head of the short flexor of the thumb Its sensory area is the ulnar border of the hand the little finger and the inner half of the ring finger

TOTAL PARALYSIS —Paralysis of the *flexor carpi ulnaris* may be detected by palpating the tendons when the wrists are flexed against resistance The limpness on the affected side contrasts strongly with the firmness on the sound side Lateral movements of the hand are unaffected as these are carried out by the extensors

Paralysis of the ulnar portion of the *flexor profundus digitorum* In making a fist flexion of the index finger is perfect and that of the middle finger good whilst in the ring and little finger it is absent or very feeble This weakness is best seen when flexion is attempted with the index and middle fingers extended Even when the fingers can be flexed by the action of the flexor sublimis the power of resisting passive extension is completely lost in the terminal phalanx of the two ulnar fingers Paralysis of the *hypothenar* muscles abolishes lateral movements of the little finger and diminishes the power of flexion at the proximal joint Paralysis of the interossei and of the inner two lumbricals leads to the production of the claw hand

The action of these muscles is to flex the fingers at the proximal joints with the distal joints extended In the claw hand the posture of the fingers is just the opposite of this namely extension at the proximal joint with flexion of the distal joints Although all the interossei are paralysed the defect is seen only in the ulnar fingers as the radial lumbricals supplied by the median are still healthy It is produced by the action of the long extensors which being now unopposed over extend the proximal joints and by the flexor sublimis which flexes the second joint and draws the distal joint down with it The clawing of the fingers is greatly accentuated when the nerve is paralysed below the point of origin of the fibres to the long flexors of the fingers Other features of the ulnar hand are atrophy of the interossei and of the hypothenar eminence and persistent abduction of the little and ring fingers

The movements of abduction and adduction are lost in the inner two fingers and often in the middle finger Further these fingers cannot be flexed at the distal joint whilst the proximal joints are extended

Paralysis of the *adductor pollicis* and of the inner head of the *flexor brevis pollicis* produces peculiar disturbances in prehensile movements If the patient is asked to grasp a folded paper between his thumb and index finger, and to resist efforts to remove it by pulling it will be found that this movement which is normally very powerful is grossly defective He cannot grasp the object beneath the thumb with the second phalanx extended, but presses the tip of the flexed thumb against the outer margin of the index finger

Sensory disturbances —In complete lesions all forms of sensation are abolished in the little finger and along the ulnar border of the hand Beyond this there is usually diminished sensibility on the ulnar side of the ring finger and over a narrow area towards the centre of the hand on both aspects Spontaneous pains are rare and vasomotor changes are usually slight.

Partial Paralysis —In partial lesions the same symptoms are found in a less degree The small muscles of the hand suffer most Clawing may be slight or absent Neuralgic pains may be felt in the distribution of the ulnar nerve but causalgia is never seen in lesions of this nerve alone

Recovery of sensation is usually complete before movement is regained The flexor carpi ulnaris recovers first then the long flexors of the fingers and last the small muscles of the hand In these recovery is extremely slow When recovery of movement is complete the patient can abduct and adduct the middle finger with the palm flat on a table and he can also scratch the table with the nail of the little finger without moving his wrist.

THE MUSCULO CUTANEOUS NERVE

This is rarely affected alone but is often implicated with the brachial plexus It supplies the biceps coraco brachialis and brachialis Flexion of the forearm can still be carried out by the brachio radialis but the power of flexion is greatly diminished Sensation may be diminished or lost along the radial border of the forearm

THE AXILLARY NERVE

This nerve supplies the deltoid and teres minor, and the skin over the deltoid It may be injured alone in injuries of the shoulder and by pressure of a crutch The chief symptom is paralysis of the deltoid with almost complete inability to raise the arm

In war injuries lesions of the nerves of the lower limb are very frequent but in civil practice apart from sciatica and foot drop local lesions of these nerves are uncommon

THE LUMBO SACRAL PLEXUS

The *lumbar plexus* may be damaged by abdominal tumours and its roots by new growth or other disease of the vertebræ In a certain number of cases signs of inflammation of the lumbar plexus are found in association with sciatica or neuritis of the *sacral plexus*

The *sacral plexus* may be damaged by growths or inflammation in the pelvis by compression during parturition and by penetrating missiles It is also often the seat of spontaneous neuritis

FEMORAL NERVE (L_2 L_3 L_4)

This is the largest branch of the lumbar plexus It supplies the iliacus pectineus sartorius and quadriceps femoris It may be injured alone by fractures of the pelvis or of the femur, by dislocations of the hip or by implication in wounds psoas abscesses or new growths

The *most prominent symptoms* are *loss* of power to extend the knee loss of the knee jerk wasting of the quadriceps and sensory disturbances over the anterior surface of the thigh and inner surface of the leg The psoas always escapes unless the plexus itself is also damaged, but flexion at the hip may be imperfect through paralysis of the iliacus *Owing to the rapid dispersion of the branches in the thigh* wounds in this part often cause partial lesions In these the *nerve to the quadriceps* is most often injured The resulting paralysis causes serious disability in walking as the knee gives way at every step, especially in going down stairs and lameness lasts for a long time after return of voluntary movement

OBTURATOR NERVE (L_2 L_3 L_4)

This nerve is rarely damaged alone It supplies the three adductor muscles the obturator externus and the gracilis The symptoms are weakness of adduction and internal rotation at the hip

LATERAL FEMORAL CUTANEOUS NERVE (L_2 L_3)

This nerve supplies an area of skin on the antero lateral aspect of the thigh As a result of injury but more often without obvious cause the skin in the territory of this nerve may show peculiar sensory disturbances which have been described under the name of *meralgia paræsthetica* Most cases occur in men In women it is usually associated with pregnancy The nerve is tender on pressure at the point where it passes from under Poupart s ligament and neuralgic pain or numbness and tingling is felt in the skin which may be slightly insensitive on objective examination or extremely hyperæsthetic so that the slightest touch causes pain The symptoms which are always unilateral are made worse by walking and may cause serious incapacity by their persistence and severity In severe cases the nerve should be excised

THE SCIATIC NERVE (L_4 L_5 S_1, S S_3)

This supplies the flexors of the leg and all the muscles below the knee It may be involved in pelvic new growths or injured by fractures of the pelvis or femur Next to the radial and ulnar it suffers in gunshot wounds more often than any other nerve

TOTAL PARALYSIS —The foot drops and the toes point downwards Walking is possible but the patient cannot stand on the heel or toes of the paralysed foot The knee is raised high but the steppage is not so marked in total lesions as when the common peroneal alone is paralysed All movement below the knee is abolished When the wound is in the buttocks flexion of the knee is very weak The foot *becomes œdematous if allowed to hang down* *Sweating is often* absent on the sole and dorsum of the foot but is normal on the inner side of the foot which is supplied by the femoral The skin is dry and thin and may be scaly Hyperkeratosis of the sole is common Subjective sensibility is rarely affected The skin is completely anæsthetic over the entire foot except the inner border of the sole and around the internal malleolus The anæsthesia extends upwards on the postero external aspect of the calf in its lower two thirds embracing the tendo Achillis and external malleolus Beyond this area of complete anæsthesia there is a wide zone in which sensibility is diminished The sense of position and passive movement is abolished in the foot and toes The knee jerk is present *The ankle jerk is always lost*

PARTIAL PARALYSIS —In wounds of the sciatic nerve it often happens that the fibres of the common peroneal alone are wounded since the sciatic trunk often divides into the tibial and common peroneal branches as high as the great sciatic notch The symptoms are described below under paralysis of these nerves In other cases the fibres of the tibial nerve are damaged either alone or with some of the fibres of the common peroneal In this case the outstanding clinical features are paralysis of the muscles of the calf and foot anæsthesia of the sole and with incomplete lesions pain similar to that described in partial lesions of the median nerve

COMMON PERONEAL NERVE

This nerve may be injured as it winds round the fibula by wounds or fractures or by compression of a tight bandage The paralysis is usually severe all the muscles being equally affected The foot is dropped and inverted and the toes are slightly flexed Dorsiflexion of the foot extension of the proximal phalanges of the toes and abduction of the foot are impossible The patient can walk and he can stand on tiptoe, but he cannot run and walking is made difficult by the foot drop Subjective sensory disturbances are usually absent The skin is anæsthetic over a narrow band which extends from the outer surface of the leg in its middle third downwards beside the outer border of the tibia and along the middle of the dorsal aspect of the foot as far as the base of the toes For an inch or so, on both sides of this band the sensibility of the skin is diminished The knee jerk and ankle jerk are present The plantar response is always flexor Vasomotor changes are slight and trophic changes are absent

TIBIAL NERVE

This nerve is rarely injured alone It supplies the popliteus the calf muscles the flexors of the toes and the intrinsic muscles of the foot When it is paralysed the patient is unable to stand on tiptoe or to extend or invert the ankle or to flex his toes Paralysis of the interossei leads to a claw like deformity of the foot associated with lowering of the heel and raising of the metatarsus—talipes calcaneo valgus The calf muscles are flabby and the ankle jerk is abolished Sensation is lost on the sole except along its inner border on the outer border of the foot and on the plantar surface of the toes Causalgia similar to that in paralysis of the median is very often present

The distal portion of the tibial nerve may be injured by a penetrating missile or a deep wound in the calf Movements of the ankle are unaffected and anæsthesia is confined to the sole of the foot and heel or merely to its inner half The paralysis of the intrinsic muscles of the foot may escape detection and the lesion may easily be overlooked especially when the nerve is injured below the origin of branches supplying the flexor longus hallucis and the flexor longus digitorum The symptoms then are pain in the sole of the foot anæsthesia on the sole and paralysis of the plantar muscles

Treatment of Local Nerve Lesions—Treatment must depend on the nature and degree of the lesion During the long period which elapses between the onset of paralysis and the first signs of recovery even in cases of simple physiological interruption of the nerves every effort must be made to prevent degeneration of the muscles to keep the circulation of the limb active and to prevent the occurrence of contractures and deformities Massage movements electrotherapy and suitable appliances all have their uses With regard to operative treatment it must be remembered that more than half the cases of nerve injuries undergo spontaneous cure It is advisable therefore to wait 3 or 4 months before an operation is undertaken If at the end of this time the wound is soundly healed and all signs of sepsis have

disappeared, and if as a result of repeated examinations, no sign of recovery has been detected no harm can be done by exposing the nerve If it is found to be divided completely the ends should be "freshened and sutured end to end If the nerve is notched laterally the edges of the notch should be pared and sutured care being taken to preserve the bridge of uninjured tissue Sometimes the nerve at the site of the lesion appears as a fibrous flattened band between two swellings on the nerve In most of such cases the nerve is completely divided, and the condition calls for resection of this fibrous tissue and end to end suture Another common finding, when the nerve is exposed, is a nodule or cicatricial swelling in the course of a nerve which has maintained its continuity In these cases the continuity of the nerve should not be interrupted It should be freed from adhesions and incised in the long axis of the swelling Operations which involve grafting of nerves have met with little success For an account of the advances in the technique of the surgical treatment of nerve injuries which have been made as a result of experience gained in the Wars of 1914–1918 and 1939–1945 special treatises must be consulted

The treatment of painful forms of nerve lesions is extremely difficult In severe cases external applications and internal medication entirely fail Simple freeing of the nerve sometimes gives relief Where this fails, it may be advisable to practise complete division followed by immediate suture In other instances sympathectomy, by excision of the stellate ganglion in the case of the upper limb and of two or more of the lumbar sympathetic ganglia in the case of the lower limb may give lasting relief

INTERSTITIAL NEURITIS

Synonym —*Neuro fibrositis*

Definition —A painful malady which commonly attacks the large nerve plexuses or nerve trunks but which may affect any peripheral nerve, and is believed to be due to inflammation of the interstitial connective tissues which surround and bind together the nerve fibres into the nerve trunks

Ætiology —It is in general a malady of middle life being unknown in childhood and uncommon in old age It is often associated with other forms of fibrositis and especially with arthritis *e g* the brachial nerves being affected in some cases of arthritis of the shoulder and the sciatic nerve in certain cases of arthritis of the hip Injury involving stretching bruising or wounding of a nerve trunk may produce it but it is necessary to bear in mind that pain following an injury even after a long interval may be the result of the rupture of an intervertebral disk which has been injured at the same time Gout diabetes and chronic nephritis are well known clinical associations of interstitial neuritis

Symptoms —These are those of irritation of the nerve fibres Pain is usually the outstanding feature It radiates in the area of distribution of the affected nerve is of a dull aching character with acute exacerbations and is often very long lasting and wearing to the patient The affected nerve is tender to pressure and stretching Subjective peripheral sensations such as tingling burning or numbness are usual and are often the first symptoms There is marked hypotonus of the muscles of the affected limb followed by a degree of general wasting not confined to the muscles supplied by the affected nerve but resembling arthritic muscular atrophy Fibrillation sometimes occurs and cramps are common The deep reflexes of the limb are increased Trophic and vasomotor changes are not infrequent.

Diagnosis —There is often considerable difficulty in the diagnosis of interstitial neuritis on account of the almost identical clinical picture which may occur in the early stages of pressure upon nerve roots or nerves by tumours or as a consequence of the irritation of one or more nerve roots by the extruded nucleus of a ruptured

intervertebral disk The special problems of the sciatic nerve are discussed under the heading of sciatica but the following points are of value in distinguishing in general between interstitial neuritis and the effects of pressure on nerves With pressure lesions the pain is rarely so severe as that of interstitial neuritis tenderness on pressure of the nerve trunks is absent and signs of loss of function—paralysis and sensory loss—come on early The most careful search should be made in every case for any possible cause of local pressure such as primary and secondary neoplasms vertebral and spinal tumours and spinal caries To make a diagnosis of interstitial neuritis in the presence of a mammary or other carcinoma or after its removal is to advocate the highly improbable whatever the symptoms may be

Treatment —The details of treatment vary according to the site of the nerve or nerves affected but the general principles are to secure rest and to avoid all those things which excite or increase the pain In most cases warmth in all forms has a beneficial and comforting effect, the part should be kept warmly clad but if special applications such as radiant heat or infra red rays excite pain they should not be persisted with Salicylates and all the analgesics of the coal tar series are valuable aids In the acute stage morphine preparations may be required to obtain sleep for the patient but later combinations of aspirin with barbiturate hypnotics suffice

CERVICO OCCIPITAL NEURITIS

This condition which is by no means rare is characterised by pain in the upper part of one side of the neck radiating over the branches of the upper cervical plexus the great auricular being the most common and the supra sternal supra clavicular and supra acromial branches less common seats for the pain The fibrositis not infrequently co involves the fibrous structures in the region of the articular and transverse processes giving rise to pain and stiffness of the neck on movement. When the pain is confined to the great occipital distribution alcohol injection is sometimes most efficacious

BRACHIAL NEURITIS

Two varieties of neuritis affect the brachial plexus and its branches namely a paralytic variety and a non paralytic the latter being one of the forms of interstitial neuritis

PARALYTIC BRACHIAL NEURITIS

This variety rare before 1939 has been common in England during recent years and occurred not infrequently in the armies abroad The cause of the condition is unknown but the course of the malady resembles that of an infective disease and in many cases the onset of the neuritis has occurred while the patients were in hospital suffering from an infectious illness of the respiratory or alimentary system

Symptoms —Severe pain in the shoulder or side of the neck radiating down the arm is usually the first symptom but in a few cases no significant pain occurs In the more severe cases general malaise accompanies the onset After a few days paralysis is noticed affecting as a rule some of the more proximal muscles innervated from the brachial plexus Paralysis of the serratus anterior with consequent winging of the scapula is especially frequent and if the patient is in bed because of other symp toms this disability may escape notice until he is up and about again and begins to u e the arm of the affected side If the paralysis affects the muscles of the upper arm wasting is soon evident All the tendon jerks of the affected arm or of both

arms may be abolished Tenderness is present over the brachial plexus and may persist for several weeks Sensory loss is as a rule slight or absent The cerebro spinal fluid is usually normal

Differential Diagnosis —This malady as a rule, only requires to be known about to be recognised, but in subjects of military age or younger the diagnosis has to be made from poliomyelitis In the latter, the onset is more abrupt and in adults is accompanied by a greater degree of malaise and fever, stiffness of the neck is usual and Kernig s sign may be present, the cerebrospinal fluid contains a considerable excess of lymphocytes, followed by a gradual rise of protein during the weeks succeed ing the onset of the paralysis The paralysis tends to have a segmental distribution whereas in the case of brachial neuritis it has much more tendency to be limited to the muscles supplied by one or two individual nerves

Course and Prognosis —In this variety of brachial neuritis the pain usually passes off within a few days and sensory loss if any is soon recovered from, but the outlook as regards recovery of the muscular paralysis is always doubtful, and if such occurs it takes many months

Treatment —The cause of the disease being unknown treatment can only be on general principles Analgesics are given for the relief of pain, and the affected limb is supported in such a position as to relax the paralysed muscles Preparations of vitamin B are often exhibited but it is doubtful whether they are of any value in aiding the recovery of the affected nerves in this disease

INTERSTITIAL BRACHIAL NEURITIS

Ætiology —This variety of brachial neuritis is somewhat uncommon and is met with chiefly in patients over the age of 40 It often arises spontaneously, but is frequently associated with arthritis in the shoulder or neck and it may follow injury to the brachial plexus from any violence causing undue separation of the head and the shoulder

Symptoms —Brachial neuritis of this variety has the general characters of inter stitial neuritis The pain which is often of abrupt onset, may be of great severity and may be at first referred to the region of the plexus itself, the back of the scapula the axilla the forearm or the hand Whatever its site the pain is at first intermittent but it soon becomes continuous and spreads over the whole upper limb Tingling and numbness in the hand and trophic changes in the skin and finger nails are the rule With minimal degrees of this form of brachial neuritis, tingling in the hand in the morning is a common symptom

Diagnosis —It may be impossible to make the diagnosis from brachial pain due to protrusion of one of the intervertebral disks in the lower cervical region (*vide infra*) Other conditions likely to cause confusion are arthritis of the shoulder and cervical rib but in neither of these conditions is there tenderness of the nerve trunks or of the plexus

Treatment —One of the great difficulties in this malady is that in the upright position the weight of the arm and shoulder carries the latter downwards and so stretches the inflamed plexus adding greatly to the pain The patient therefore should be kept in bed and in general on his back Further every movement of the hand or arm tends to increase the pain, and splints which keep the arm in the abducted position and the shoulder raised so as to prevent tension upon the plexus are in valuable

BRACHIAL PAIN DUE TO A PROTRUDING INTERVERTEBRAL DISK

In a considerable number of cases brachial pain which would in the past have been diagnosed with confidence as due to brachial neuritis is in fact the result of irritation of one or more cervical nerve roots by a displaced intervertebral disk

In such cases the onset of pain is usually sudden and often follows forceful movement of the neck or prolonged strain on the cervical muscles with the head partially rotated as may occur in supporting a heavy weight

The pain is usually described as being intense in severity and is felt across the base of the neck and between the shoulder blades and is usually worse on one side It is aggravated by movement or jarring of the neck or by straining

After a few days the cervical pain usually abates somewhat in severity but pain extends down the arm to the digits on one or other side of the hand

When examined the patient is found to have considerable limitation of movement of the neck and may show severe signs of a radicular lesion in the arm in the form of muscular wasting or weakness sensory impairment and diminished reflexes The root most commonly affected is the sixth cervical and the patient s chief complaint is of pain in the arm and pain tingling and numbness in the index finger and to a less degree in the thumb on examination some sensory impairment is found over the index finger and the triceps jerk is diminished or lost and after a time some diminution of the muscles of the forearm is apparent on comparison with the normal limb

Such cases usually recover gradually with symptomatic treatment but some stiffness of the neck may remain Recovery can often be greatly accelerated by manipulation of the neck combined with axial traction which should only be carried out by an expert in manipulative methods

CERVICAL RIBS

Ætiology —The development of the ribs at the thoracic inlet depends on the mode of formation of the brachial plexus for the nerves are large structures in the embryo at a time when the ribs are soft and pliable When the plexus is normal a well formed first rib springs from the first dorsal vertebra If however the plexus is post fixed , that is when the contribution to the plexus from the fourth and fifth cervical segments is small and the fibres from the first and second dorsal segments form a powerful cord this cord in rising over the first dorsal rib may compress and deform it to such an extent that it presents the characters of a rudimentary rib On the other hand and this is more frequent when the plexus is pre fixed that is when the contribution from the upper cervical segments is relatively large and that from the dorsal segments is small a supernumerary rib is allowed to develop from the seventh cervical vertebra When this pre fixation is pronounced the seventh cervical rib is often very large and is easily felt in the neck and in these cases symptoms are usually absent In a certain number of cases in which the abnormality is intermediate in degree symptoms are caused by compression of the lower cord of the plexus as it passes over the supernumerary rib or over the deformed first rib This compression may be exercised by the bony portion of the extra rib but more often the nerves are damaged by a fibrous prolongation of the rudimentary rib which connects it with the first rib

But these abnormalities in the ribs only cause symptoms in some 10 per cent of the cases in which they are present Further the symptoms are often unilateral with bilateral supernumerary ribs and the symptoms are often most prominent on the side of the smaller extra rib Again the onset of symptoms is usually delayed until adult life is reached It is clear therefore that some contributory cause must come into play This is found in the dropping of the shoulder girdle which is normal in adolescents and is often excessive in persons whose muscular tone is low In a child the clavicle rises boldly as it passes outwards In a normal adult male the clavicle is almost horizontal in women it droops slightly and in those who develop symptoms of pressure on the nerves the outer is usually distinctly lower than the inner end

In the latter the lowest cord of the plexus is submitted to constant rubbing against the extra rib which rises and falls during respiration and it is compressed by any movement of the arm which depresses the shoulder girdle Relief is obtained by raising the shoulders and patients soon learn to support the limb and to assume attitudes in which pressure on the nerves is relieved

Women suffer most often the right arm being affected more often than the left The onset is usually gradual but occasionally it comes on suddenly after childbirth, or on lifting a heavy weight

Symptoms—These may be sensory motor or vasomotor, either singly or in combination Subjective sensory disturbances are most frequent. They take the *form of numbness and tingling* or neuralgic pains Paræsthesiæ are most often unilateral and are frequently confined to the ulnar or to the radial side of the hand and fingers It is rare for all the fingers to be affected Pain when present is usually felt below the elbow It is often neuralgic darting down the arm and again confining itself to one border of the limb *It hardly ever radiates from the neck*

Objective sensory disturbances are usually slight or absent They may be found over the ulnar or radial border of the distal portion of the limb in an indefinite area which does not conform to the distribution either of the ulnar or radial nerve

Muscular atrophy is not so frequent as *subjective sensory disturbance* In the "median type", wasting is confined at first to the abductor and opponens pollicis muscles and the outer part of the thenar eminence shows a remarkable reduction in size which contrasts strongly with the inner part, which retains its normal bulk In the ulnar type wasting appears first in the small muscles of the hand supplied by the ulnar nerve In some cases all the muscles of the hand and to a less degree the flexors in the forearm show considerable wasting The atrophy is frequently bilateral and symmetrical

Vasomotor disturbances are very common The hands feel hot or cold, they may be œdematous or discoloured and the changes may suggest Raynaud s disease Pressure on the subclavian artery sometimes causes inequality of the pulse and the pulse on the affected side may be obliterated by depression of the shoulder The inequality disappears when the arm is raised

Diagnosis—The presence of pain paræsthesiæ or vasomotor *disturbances in* the upper limbs or wasting in the muscles of the hands should always arouse the suspicion of supernumerary or rudimentary ribs When pain is the only symptom its distribution along one border of the arm or hand and the patient s account of the manner in which it may be increased or diminished by raising the shoulder girdle or performing movements which depress it usually direct attention to the cause Symmetrical atrophy in the hands may suggest progressive muscular atrophy of spinal origin but this diagnosis is usually rendered untenable by the association of sensory troubles or vasomotor phenomena or by the findings on radiographic examination of the neck For the differential diagnosis from syringomyelia see p 1547 Symptoms indistinguishable from those which commonly result from the presence of a cervical rib occur in a small number of patients in whom no cervical rib is present In most cases of this kind, the patients have very sloping shoulders and the symptoms are believed to be due to *compression of the roots of the brachial plexus between the fibre bundles of the scalenus anterior muscle In other cases either because of the* lowness of the clavicle or because the first rib is unduly high the subclavian artery is compressed between these two bones when the corresponding arm hangs down or when *it is* raised and abducted Obliteration of the circulation causes a numbness in the hand and forearm which comes and goes according to the posture of the arm The numbness may become persistent because of thrombosis at the site of compression and the patient may first come for advice when this has occurred Aneurysm is another occasional consequence of the damage to the artery

Treatment—Pain may be relieved by rest *with the arms suitably supported*

Atrophy calls for operation to remove the offending rib Pain is always relieved by operation either immediately or after an interval of some months The progress of atrophy is always retarded and complete recovery may occur if an operation is under taken early

ACROPARÆSTHESIA

Definition —Acroparæsthesia is the name given to a syndrome of uncomfortable tingling in the extremities without demonstrable sensory loss or other abnormal physical signs

Ætiology —It is unusual for all four limbs to be affected acroparæsthesia in the arms is much commoner than that in the legs In the arms it is almost limited to women whereas in the legs it is much commoner in men There seems to be an hereditary element in its causation As first described it was associated with arthritis and it seems to be commoner in arthritic subjects but both maladies occur in the same age group In both sexes the condition usually comes on in middle life but it also occurs in younger women during pregnancy

Symptoms —The tingling may be present at all times but it occurs above all during the night and wakens the sufferer from sleep some patients complain of the inability to sleep as much as of the discomfort The tingling is in some way due to the use of the limbs during the day in vigorous work or in continuous standing or car driving and if the patient rests throughout the day he or she is as a rule soon relieved of his nocturnal symptoms Many of the patients are middle aged women who have been compelled to do vigorous housework to which they have not been accustomed from youth In general warmth aggravates the tingling and the sufferer who is awakened in the night puts the affected limbs outside the bedclothes In the less severe cases the symptoms are worst during the early part of the night and after a number of hours of broken sleep the patient is able to sleep without interruption for the rest of the night In other cases the symptoms continue throughout the night and are still present in the morning then the hands may appear, or may feel swollen and the patients complain of awkwardness of the fingers but impairment of postural or other sensation can rarely be demonstrated

The symptoms are subject to long remissions but the liability to them is not often completely lost

Diagnosis —There are no objective signs of nervous or vascular disease The most careful examination must be made to exclude such causes of paræsthesiæ as sub acute combined degeneration and early polyneuritis (*e g* diabetic or lead) If the tingling is limited to a part of the hand it may be due to compression of the median nerve in the carpal tunnel or to disturbance of the ulnar nerve or to com pression of a nerve root by an intervertebral disk Slight wasting of muscles may give a clue to the presence of some organic disease The state of the pulses in the affected limbs may suggest the presence of a vascular disturbance to which the symptoms are attributable

Treatment —As has been stated the tingling as a rule ceases if the patient does no work but social circumstances rarely make continued leisure possible the patient may however be able to find more suitable employment or to make changes in his or her habits of work or a holiday particularly with sea-bathing may initiate a remission Sponging the affected limbs with cool water once or twice in the day and possibly at night gives considerable relief in most cases The combination of aspirin gr 10 with phenobarbitone or other hypnotic taken at bedtime enables the patient to sleep

SCIATICA

The term sciatica is applied in a somewhat imprecise manner to conditions in which pain is experienced along the course and in the distribution of the sciatic

nerve—that is to say in the buttock back of the thigh, outer side and back of the leg and the outer border of the foot It is important at the outset to notice the limitations of this distribution and in particular to notice that the sciatic nerve does not supply any structures on the front of the thigh and so pain in that region or in the groin is not included in sciatica

Cases of sciatica as thus defined are common and many of them have a prolonged course and other well described features Until recent years they were all confidently attributed to interstitial neuritis (sciatic neuritis) but it is now recognised that while a number are probably due to this cause many are the result of irritation of one of the roots of the great sciatic nerve by the extruded nucleus of a ruptured intervertebral disk, and others are cases of referred pain in the sciatic distribution The differential diagnosis between these different varieties of sciatica is frequently a matter of great difficulty and in fact in many cases it cannot as yet be made with confidence

SCIATICA DUE TO PROTRUDING INTERVERTEBRAL DISK

Sciatica is the syndrome to which herniation of the nucleus pulposus of a lumbar intervertebral disk most commonly gives rise

Ætiology—The majority of cases give a history of injury at, or shortly before the onset of symptoms The injury is commonly of the variety known as a strain of the back due to sudden bending the lifting of heavy weights or sudden movements of the back as when striving to avoid a fall Males are more commonly affected *In females childbirth especially with instrumental delivery is an additional cause*

Pathology—Formerly the condition under discussion was one recognised on laminectomy, and spoken of as endochondroma of the disk Actually in the circumstances enumerated above the disk ruptures and its nucleus (nucleus pulposus) subsequently herniates into the vertebral canal The commonest site of such a lesion is in the lumbar spine below the termination of the spinal cord and the extruded mass causes irritation and compression of one or more of the roots of the cauda equina The disk most frequently ruptured is that between the fifth lumbar vertebra and the sacrum (fifth lumbar disk) and the spinal root affected is the first sacral The fourth lumbar disk is also commonly ruptured and the third lumbar occasionally so *The rupture of higher lumbar intervertebral disks is infrequent* In each case the spinal root most affected is that emerging just below the site of the lesion *e g* the fifth lumbar root when the fourth lumbar disk is ruptured and so on Multiple ruptures are not very uncommon

Symptoms—The outstanding feature is pain It begins in the small of the back either at the time of the injury or after an interval of some hours days or weeks It may remain limited to the back but in most cases it extends after a variable interval down the back of one thigh and then down into the leg and possibly into the foot so that the clinical condition becomes one of sciatica The exact distribution of the pain in the leg depends on which spinal root is affected (*vide infra*) The pain is *severe and lancinating aggravated by stooping by coughing and sneezing* and by turning in bed and relieved by lying still Flexion of the extended leg at the hip is always painful (Lesegue s sign) and the patient adopts an attitude of partial flexion of the affected limb at the knee and hip which avoids tension on the sciatic nerve and its roots

The objective physical signs fall into two groups namely (1) those referable to the spine and (2) those due to impairment of function in the affected nerve root or roots The lumbar spine is *flattened and is tilted at the site of the lesion* the tilt is usually away from the side of the sciatic pain but may be towards it and in some cases the tilt alternates Radiographic examination reveals the flattening of the lumbar curve and the tilting more clearly and it may show a suggestive reduction of one intervertebral space but this is not usual The nervous signs are in general those

of impairment of function of a single spinal root Most commonly the first sacral root is the one involved and the signs which develop are as follows The ankle jerk is abolished The muscles of the calf and the peronei become slightly wasted and the change in outline is apparent when the two legs are compared with the patient standing up or lying prone The power of flexion of the small toes is diminished The glutei on the affected side are flattened Sensation is impaired along the outer border of the foot and on the outer half of the sole and the patient has a sensation of numbness or tingling in this area The impairment of sensation may be a loss or weakening of pain appreciation and loss of tickle on the affected area of the sole, or a loss of light touch appreciation, or a loss of sense of position of the small toe or all of these combined When the fourth lumbar disk is ruptured and the fifth lumbar root is consequently most affected the site of the worst pain is on the outer side of the leg and perhaps on the dorsum of the foot, wasting of the calf is less pronounced and the ankle jerk is more often diminished than abolished, an area of sensory loss for light touch or impairment of pin prick appreciation may be found on the outer side of the calf In severe cases some disturbances may be found in the functions of the first sacral root as well as in those of the fifth lumbar With lesions of the higher lumbar disks the pain is maximal in the fourth or higher root distributions and the knee jerk may be diminished or lost

It should be borne in mind that in a proportion of cases the nervous symptoms are entirely irritative and consequently objective signs due to impaired root function are lacking Spinal signs are usually present and ultimately some wasting appears but in a number of such cases it is as yet impossible to make the differential diagnosis from sciatic pain due to other causes

Diagnosis —When the diagnosis is in doubt special radiographic examination after injection of Myodil into the theca shows a filling defect in the Myodil shadow corresponding to the knuckle of cartilage indenting the theca This method of investigation is not infallible but in the present state of our knowledge its results should be taken as a practical guide

In almost every case the problem is to distinguish the symptoms of a ruptured intervertebral disk from sciatica due to other causes Most cases of sciatica in people under 40 years of age are due to ruptured discs As age increases other causes assert themselves more strongly but in people who are of athletic type given to such forms of physical activity as gardening horse riding and golf and who are free from arthritis ruptured disk is always a likely cause If there is some history of injury or strain if both the spinal and nervous groups of signs are present and if the latter are limited to the distribution of a single root there is little doubt about the diagnosis In cases of sciatic neuritis tenderness along the line of the sciatic trunk is pronounced and pain and tenderness are seldom limited to the distribution of a single spinal root In cases of referred sciatic pain reflex changes muscular wasting and objective sensory loss are absent Very prolonged and especially recurrent sciaticas are mostly due to ruptured intervertebral disks

Course and Prognosis —In the absence of operative treatment the symptoms usually subside gradually in the course of from 6 weeks to 6 months In a very few cases they clear up more quickly and in quite a number they persist in some degree for years sometimes better and sometimes worse The muscular wasting though obvious never becomes severe and there is never total paralysis of the affected nerve root

Treatment —It is not known how the structures within the vertebral canal adapt themselves but in most instances the pain subsides without operative removal of the protruding mass It is to be presumed that the affected nerve root suffers the minimum of physical irritation when the patient takes up the posture which is for him least painful In general the patient should remain at rest in his most comfortable position and be given such pain relievers of the nature of aspirin veganin and

the like, as may be necessary, together with sedatives if called for In the most acute cases an injection of morphine gr ¼ or pethidine 100 mg may be necessary at night but both these drugs should be used with great care because of the danger of addiction Physiotherapy may be comforting after the acute phase has passed but it is doubtful whether it has any curative effect When the patient has been free from pain for a week while still in bed he may be allowed to sit up and very gradually begin to move about but he should avoid doing anything which causes pain and he should rest when pain begins If pain is recurrent when the patient has begun to move about, support of the lumbar spine by a plaster jacket may give relief

Operation for the removal of the protruding portion of disc is advisable (1) if after 6 weeks or so the pain is not definitely diminished (2) if the sciatica is recurrent (3) if the patient s employment involves heavy work and much movement of the back The operation is not a severe ordeal and most patients are walking again within 3 weeks In general the results are excellent but in some cases some pain persists or returns

REFERRED SCIATIC PAIN

In some cases of sciatic pain there are no manifestations of disease of the sciatic nerve itself either in the way of impaired function or of tenderness and the pain is believed to be a referred pain excited by disease of other structures within the nerve distribution of the spinal segments from which the sciatic nerve arises Such pain is abolished by the cure of the primary disease or anæsthetisation of the structure which it affects Conditions which may give rise to referred sciatic pain are arthritis in the hip joint, arthritis in the sacro iliac joint disease of the lower lumbar vertebræ or of the sacrum, trauma of the gluteal muscles and lesions of the vertebral ligaments It should be noted that malignant disease of the lower vertebral bones may cause severe referred sciatica at a time when no bony change is revealed by radiography and the occurrence of sciatic pain in a patient who has suffered from carcinoma is to be interpreted in the light of this knowledge Elliott and Weddell have shown that the presence of so called rheumatic nodules in the gluteal muscles is not to be regarded as evidence of fibrositis there which might excite sciatic pain because the nodules are due to local muscular spasm consequent upon irritation of nerve fibres, and are not primarily a rheumatic manifestation

Referred sciatic pain is usually moderate in intensity Its distribution is usually in the calf or on the outer side of the leg or on the outer side of the ankle The calf muscles are slightly tender and are the seat of discomfort which causes the patient to make movement of them at frequent intervals The absence of all signs of impaired nervous function has already been mentioned and is the most important diagnostic feature

In all cases of referred sciatic pain the treatment is that of the exciting condition Injection of a local anæsthetic into the disordered structure abolishes the pain temporarily and occasionally the relief is permanent especially if the anæsthetic is used in oily solution the effect of which is more lasting than that of an aqueous solution

OBSTETRICAL PARALYSIS

It is important and useful to group together under this heading all those conditions of paralysis occurring either in mother or child which are the result of the processes of labour in the passage of the fœtal head through the pelvis Autopsies upon the still born and upon children who have survived birth for a few days only have shown that hæmorrhage into the meninges is of common occurrence and it has been argued that such meningeal hæmorrhages are the cause of many of the conditions of cerebral paralysis which are present immediately after birth or which appear during the first

year of life and especially the cause of cerebral diplegia The pathological conditions found in the brain in cases of cerebral diplegia however are such as make it impossible that they could be caused by meningeal hæmorrhage, for no sign of old hæmorrhage is ever found nor could hæmorrhage cause a general cell atrophy of the brain without signs of any local lesion It seems clear, then that though meningeal hæmorrhage may be of common occurrence during birth, and may be the cause of still birth yet there is no clinical or pathological evidence to show that it gives rise to any lasting cerebral defect

The following conditions may occur (1) In the child facial paralysis hemiplegia from laceration of the brain substance fracture-dislocation of the spine with transverse lesion of the spinal cord injury to the brachial plexus from the separation of head and shoulder in traction and injury to peripheral nerve trunks at the elbow, axilla or groin in using traction with the finger

(2) In the mother paralysis of the supply of the lumbo-sacral cord and obturator nerve from prolonged pressure of the head against the sacrum and pelvis.

Facial paralysis —This is usually caused by the pressure of the forceps upon the facial nerve as it crosses the ramus of the jaw but it has been known to occur where instruments have not been used When unilateral as is the common event it gives rise to little or no difficulty with sucking and is evidenced by the unsightly deformity of the face which is drawn over to the sound side When bilateral it is one of the causes of complete inability to suck and on account of the flaccid symmetry of the face may easily be overlooked It necessitates spoon feeding for a considerable time Obstetrical facial paralysis invariably recovers within a few weeks and does not give rise to after contracture Gentle stretching and massage of the face with the finger is the only treatment required

Hemiplegia from laceration of the brain may occur during delivery in contracted pelvis from the pressure upon the sacral promontory and has been caused by the use of *forceps It is exceedingly rare and is generally rapidly fatal from the associated* hæmorrhage It may occasionally be survived with an irreparable hemiplegic condition

Fracture dislocation of the spine is produced by traction upon the aftercoming head by pulling upon the trunk, and it may be associated with injury to the brachial plexus It occurs most often in the lower cervical region and the transverse lesion of the spinal cord is usually complete

Injury to the brachial plexus may occur in traction either upon the head or upon the trunk if the head is aftercoming and is caused by an undue separation of head and shoulder on one side rupturing or straining the brachial plexus The paralysis is usually of the upper arm or Erb type the fifth and sixth roots being most affected, and the deltoid biceps and supinator longus muscles being paralysed but the whole plexus may be involved and even torn completely across Traction upon a prolapsed arm has caused lower arm or Klumpke type of paralysis in which the first dorsal and eighth cervical *roots are most affected* and the intrinsic *hand muscles* and the flexors of the forearm are paralysed The obstetrical lesions of the brachial plexus are for the most part serious lesions many of the cases making no motor recovery at all though sensibility is usually regained The prognosis depends upon the severity of the damage to the plexus as to whether the roots are actually torn or only bruised The slight cases recover well enough

Injury to the peripheral nerves from pressure or traction upon the flexures is seldom severe enough to prevent a rapid and complete recovery

Paralysis of the lumbo sacral cord and of the obturator nerves in the mother immediately after parturition is an exceedingly interesting clinical condition In the first place the lumbo sacral cord is in a much more exposed position as regards the fœtal head engaging the pelvis than are the other nerves of the sacral plexus and may be subjected to such severe pressure as causes paralysis and in the second place

the obturator nerve actually crosses the brim of the pelvis and must of necessity be pressed upon by any large fœtal head which passes the pelvic brim The lumbo-sacral cord paralysis is evidenced by dropped foot and paralysis of the anterior tibial and peroneal muscles and if it is severe by loss of sensibility over the distribution of the fourth and fifth lumbar roots Sometimes the third lumbar root area is affected The obturator nerve involvement is shown by weakness or paralysis of the muscles supplied by the obturator nerve, namely all the adductor muscles of the thigh The paralysis may be noticed directly after parturition or when the patient begins to get about upon her legs The lumbo sacral paralysis is usually unilateral and is nearly always upon the right side The obturator paralysis is not uncommonly bilateral, and both forms of the paralysis may coexist There may be numbness but no pain This condition nearly always occurs with a first delivery, and often the child s head has been unduly large It may recur with subsequent deliveries, but this is not a common event

The *prognosis* is absolutely favourable, every case making a complete recovery in from a few weeks to a few months The treatment is rest in the first place with gentle massage and passive movements, and when power begins to return the patient may commence to get about

POLYNEURITIS

Synonym—Multiple Peripheral Neuritis

Introduction—The clinico pathological condition known as polyneuritis and seen in its most typical form in diphtheritic paralysis or in alcoholic neuritis represents a very striking and uniform reaction of the nervous system Invariably associated with it is a reaction of the myocardium so that there is in cases of polyneuritis a recognised liability to sudden fatal heart failure It is in diphtheritic paralysis and beriberi another form of polyneuritis that this mode of fatal termination is most often seen Indeed beriberi may appear as a rapidly fatal cardiac illness before any signs of involvement of the nervous system have had time to develop

Ætiology—At first sight the factors that give rise to polyneuritis fall into three groups (i) certain chemical poisons (ii) the toxins of certain bacteria and (iii) certain disorders of metabolism Widely differing as these three causative factors may seem to be, there is reason to believe that a common underlying factor which is immediately responsible for polyneuritis may underlie them all It is probable that in the case of groups (i) and (ii) the pathogenic substance gives rise to a disorder of metabolism in the course of which a toxic metabolite is produced in the body this acting as the direct poison for nervous system and heart muscle In the metabolic group (iii) the same process is in action Thus in beriberi for example the illness ensues upon the ingestion of a diet deficient in vitamin B_1 In the absence of this substance carbohydrate metabolism is disordered and a toxic metabolite is produced Thus beriberi is not as the biochemists formerly insisted a starvation degeneration of the nervous system but an intoxication strictly comparable with that obtaining in other varieties ætiologically considered of polyneuritis The final and complete proof of this unity of causation of polyneuritis in whatever circumstances it is seen is not yet available but there is an increasing body of evidence in favour of it

Returning to the ordinary ætiological classifications of polyneuritis we see that in alcoholic or arsenical polyneuritis the poison is taken by the mouth and presumably the final common toxic substance reaches the nervous system by the blood stream In diphtheritic paralysis on the other hand the exotoxins are produced locally at the site of the diphtheritic ulceration whether on the fauces or as in extra faucial diphtheria at some other local site on the body surface This unique channel of entry gives rise in diphtheritic paralysis to a group of symptoms not found in other

ætiological varieties of polyneuritis This group includes palatal and accommodation paralyses which precede the appearance of polyneuritis It is noteworthy that in the case of extrafaucial diphtheria this initial paralysis is not palatal but is anatomically related to the site of the diphtheritic lesion (skin ulceration or wound) Yet the paralysis of accommodation may occur whatever be the site of the diphtheritic lesion It is believed therefore that the exotoxins gain access to the nervous system by conduction from the seat of the lesion via the axones of the nerves which innervate this region They pass upwards in the axis cylinders to the central nervous system and produce their toxic action directly there this action being reflected peripherally again as a motor and sensory paralysis of the muscles and skin (or mucosa) in the region of the lesion Thus a diphtheritic ulcer on a finger may be followed by a local paralysis of that part before polyneuritis develops The subsequently developing polyneuritis is then probably produced in the manner described above while the accommodation paralysis may indicate a specific action of the toxin upon the nervous mechanism concerned We thus have a local a specific and a general group of symptoms The analogy of the local specific and general phases of tetanus will occur to the reader

A peculiar effect of abnormal metabolism is the occurrence of polyneuritis in association with bronchial carcinoma

Acute febrile polyneuritis and Landry s paralysis have no known causal factors They make their appearance in apparently healthy persons adequately nourished and free from all discoverable signs of infection and it is extremely difficult in the present state of knowledge to account for them on any hypothesis of avitaminosis or to suggest any possible mode of intoxication

Many of the intoxications of the nervous system commonly included under the heading of polyneuritis are associated with lesions and clinical manifestations which are not those of polyneuritis Such substances to name but a few are lead, mercury copper carbon disulphide and carbon monoxide and it would be erroneous to regard these as causes of polyneuritis

Pathology —The changes in the nerves are those of parenchymatous neuritis and longitudinal sections stained by the Marchi or Weigert Pal methods show severe degeneration of the fibres The alterations are most intense in the small branches supplying the skin and muscles and they diminish in severity as the larger branches are approached They are best seen in the terminal branches of the musculo spiral and anterior tibial nerves The wasted muscles often show a reduction in the size of their fibres and an increase of connective tissue—fibrous myositis The spinal cord may be healthy but in almost all cases examination by modern methods shows changes in the nerve cells and degeneration in the tract fibres derived from the posterior roots

Symptoms —As might be expected from the composition of the peripheral nerves the symptoms of polyneuritis may consist of disorders of movement sensation and autonomic function and these disorders are symmetrical and typically begin in the peripheral portions of the limbs and spread proximally The relative severity of these disturbances varies from one variety of polyneuritis to another and the detailed symptomatology of each variety is more fully considered below The motor disorder is in all instances a lower motor neurone paralysis with the characteristic weakness, reflex loss and tendency to wasting of the muscles a marked propensity to contracture is universal Bilateral drop foot is in a large number of cases the first objective motor manifestation The sensory disorders are similarly peripheral and symmetrical and may involve both superficial and deep sensibility and may be both positive (pains and paræsthesiæ) and negative (anæsthesiæ) The first complaint is usually of numbness in the feet and in the hands and this extends proximally and is soon accompanied by objective sensory loss which by reason of its mode of development soon has char acteristically a glove and stocking distribution In some varieties the autonomic

defects are seen in alterations in sweat secretion and trophic changes in the skin, nails and other tissues

The tendency to myocardial weakness which has already been mentioned, though characteristic only of certain varieties should be borne in mind in all cases

The cerebrospinal fluid in the infective types of polyneuritis contains an excess —usually a great excess—of protein the globulin fraction also showing an increase, the other elements of the fluid are normal except that in rare cases of acute infective polyneuritis cellular increase may be found

Diagnosis —The diagnosis of polyneuritis from other diseases rarely presents serious difficulty It is made from the combination of symmetrical flaccid paralysis with sensory loss of the "glove and stocking" distribution, and tenderness of the muscles and nerves, confined to or most intense in the distal part of the limbs A variable degree of polyneuritis is an associated feature of subacute combined degeneration of the spinal cord and this disease may easily be confused with polyneuritis The differential clinical features are given on p 1553 and as pointed out there, the distinction at an early stage may in some cases be made with confidence only by examination of the blood for the characters of pernicious anæmia The development of extensor plantar reflexes is an absolute point against polyneuritis while a great excess of protein in the cerebrospinal fluid is equally against subacute combined degeneration When sensory disturbances and diminished tendon reflexes are prominent symptoms and muscular weakness is slight *tabes* may be suggested and the resemblance is still greater when ataxia is present Difficulty usually arises when the distinction has to be made between tabes and alcoholic neuritis in a patient who has courted both diseases In most instances the diagnosis can be made from the nature and distribution of the sensory changes The lightning pains of tabes cannot be mistaken by anyone who is familiar with their peculiar characters Anæsthesia of the extremities is common to both diseases but diminished sensibility around the nose and across the chest is peculiar to tabes and is present in almost every case In neuritis the calf muscles and nerve trunks are tender, whereas in tabes the sensibility of these structures is usually greatly diminished Hyperæsthesia to touch and temperature and great exaggeration of the abdominal reflexes also suggest tabes Examination of the cerebrospinal fluid usually puts the diagnosis beyond doubt.

Rarely does polyneuritis come on with such rapidity as to simulate poliomyelitis When it does so the occurrence of any peripheral sensory loss may reveal its nature, and the absence of cells in the cerebrospinal fluid shows that the illness is not poliomyelitis

Course and Prognosis —In a few instances myocardial failure or respiratory paralysis brings about a fatal issue at the height of the illness Otherwise the normal course of the disease is a stage of invasion followed by a stage of recession leading to complete recovery The duration of these varies greatly according to the ætiology of the malady In rare cases recovery fails to occur and in the chronic hypertrophic types of the disease this is the rule

Disability after recovery from the neuritis may result from muscular contractures wasting or neuritic pains

Treatment —The first essential is to remove the patient from the influence of the exciting cause In alcoholic cases, rigid precautions are necessary to prevent secret access to alcohol To attain this treatment in an institution is almost a necessity In most instances when the cause whatever it may be is removed gradual improvement sets in and complete recovery ensues, in a time that varies with the severity of the symptoms During this time the physician s most important duty is to prevent the occurrence of deformities and contractures From the beginning each joint in the affected limbs should be moved passively to its full range several times each day and care should be taken to ensure that the attitude of the limbs during rest is a suitable one especially that the feet are maintained at right angles to the legs by the use

of appropriate apparatus Drawing up of the heel must be prevented at all costs

Gentle massage is soothing in the acute stage provided muscular tenderness does not preclude it Later more vigorous rubbing may be given and the patient should be encouraged to move the limbs voluntarily Electricity is seldom called for Analgesic drugs and soothing applications may be needed at the onset Thereafter local treatment to the limbs is combined with measures to improve the patient s general condition

The administration of vitamin B_1 preparations has now a great vogue in the treatment of both multiple (parenchymatous) and interstitial neuritis In the latter its use has no theoretical justification or practical value and even in the former though its use is rational it yet remains to be proved that the course of the malady is materially influenced This may be due to inadequacy of dosage in the past, and the parenteral injection for from 2 to 4 weeks of 1000 to 2000 units daily is the minimum dosage likely to be efficacious Even with this dosage it is not yet clear that the course of any ætiological variety of polyneuritis is materially influenced, and extravagant claims should be treated with great reserve

ALCOHOLIC NEURITIS

In former years alcoholism was perhaps the commonest cause of severe peripheral neuritis but at present alcoholic polyneuritis is a rare disease in the British Isles It occurs most often in women especially in those who take small amounts of alcohol frequently and it has often been the first indication of secret drinking There is much evidence that the disorder results as much from the deficient diet and the chronic gastritis commonly found in alcoholic subjects as from the direct toxic effect of the alcohol taken

The onset is insidious, and in most cases premonitory symptoms such as numbness and tingling in the extremities or cramps in the muscles of the lower limbs are present for several months before actual weakness occurs Subjective sensory troubles are a marked feature even in the early stages Besides numbness and tingling the patients complain of feelings of excessive heat or of coldness in the limbs or of severe aching or cutting pains in the legs Painful cramp in the calf muscles is a common symptom It is often worst at night and may interfere seriously with sleep Objective examination usually reveals sensory loss in which the various elements of sensation are affected in a manner which is almost pathognomonic

Stated briefly there is anæsthesia of the skin with hyperæsthesia of the deeper structures Light touches are not appreciated at all or many are missed the temperature sense is defective and the prick of a pin causes no pain whereas even moderate compression of the muscles may cause the patient to cry out The sensory loss is greatest in the feet and hands and diminishes towards the knees and elbows Muscular tenderness is usually greatest in the calves The soles of the feet are also unduly tender Hyperalgesia is often well marked before anæsthesia of the skin appears To the disability caused by pains and spasms weakness of the muscles is added in all but the slightest cases The arms may suffer first but in most cases the extensors of the toes the dorsiflexors of the ankle and the extensors of the fingers and wrists are attacked in progression and double foot drop and wrist drop result To overcome the foot drop the knees are raised high in walking This gives to the gait the steppage character which is common to all forms of peripheral neuritis In most cases the distal flexor muscles are also affected but to a slighter degree In severe cases weakness extends to the proximal muscles and even to the muscles of the trunk The affected muscles become soft and diminish rapidly in bulk Unless precautions are taken, contractures occur in the flexor muscles and produce deformities of the limbs which add greatly to the difficulties of treatment

At the onset the knee jerks are exaggerated but in most cases by the time the patient comes under observation all the tendon reflexes are absent The cutaneous reflexes may be unaltered, diminished or absent Sphincter control is retained Slight bilateral weakness of the face is often present but severe paralysis is rare Ptosis nystagmus and weakness of the external ocular muscles have been observed

Trophic and vasomotor disturbances in the extremities are common The hands and feet often perspire freely at first and then become unnaturally dry, and they may be white and cold or red and hot In some cases œdema of the hands or lower extremities is present In chronic cases the skin of the hands and fingers is thin, smooth and shiny, and the nails are ridged and brittle

In almost every case of alcoholic neuritis there is some *psychical defect* One form—Korsakoff s psychosis—is characteristic of and almost peculiar to this disease The most prominent feature is failure of memory for recent events and loss of appreciation of time and place A patient who has been bedridden in a hospital for nervous diseases for several weeks when visited by the resident physician who has attended her daily will recognise' him at once as Dr X, whom she has not seen since he brought her first child into the world some years ago She is now she says in a lying in hospital which she entered yesterday and has just been confined with her second baby, who is in bed beside her She also recognises strangers at her bedside and connects them with events of long ago Everything is related in the most circumstantial manner, and if the facts were not known her tale might well be accepted as truth In most cases the mental defects are not so gross There is merely a failure of memory, to which is added moroseness and irritability caused by withdrawal of alcohol

ARSENICAL NEURITIS

Peripheral neuritis may be caused by a single large dose of arsenic or it may result from prolonged use of the drug in the treatment of such diseases as Hodgkin s disease chorea and severe anæmia It is a rare malady and the likelihood of its appearing under the last named conditions is negligible The toxic action of arsenic with alcohol seemed to be greater than that of either alone

The description given of alcoholic neuritis applies to this form as well Hyperæsthesia of the skin and tenderness of the muscles are more constant and more severe in the arsenical form and paralysis and atrophy of the muscles are often more wide spread and more rapid in their progress Hyperkeratosis of the soles and pigmentation of the skin are characteristic of arsenical poisoning In a suspected case the diagnosis can be confirmed by the discovery of abnormal quantities of arsenic in the urine or in the hair and skin

The mental changes described in connection with alcoholic neuritis under the heading of Korsakoff s psychosis may be present especially when repeated poisonous doses of arsenic have been taken

DIPHTHERITIC PARALYSIS

The exotoxin of diphtheria is highly selective for nervous tissues and some form of paralysis occurs in a very high proportion of the cases The intensity of the paralysis bears no constant relation to the severity of the local infection for cases in which the original disease has passed unnoticed may be followed by serious damage to the nervous system Walshe has classified the nervous manifestations of diphtheria into three distinct groups namely the local the specific and the generalised paralyses

Local paralysis occurs in parts related anatomically by nervous connections to the site of the diphtheritic lesion In faucial diphtheria the local palsy appears in the palate In extra faucial diphtheria *e g* infected sores on the limbs the local palsy appears in the muscles supplied by the segments of the cord to which afferent nerve

from the infected focus pass The reason for this is that toxins elaborated by the diphtheria bacillus ascend from the primary focus to the cord or the medulla Having reached the central structures they diffuse to neighbouring motor cells and by injuring them cause paralysis of the muscles they supply Paralysis of the palate therefore does not occur except in faucial diphtheria

The *specific manifestation of diphtheria is paralysis of accommodation* Like trismus in tetanus it is not due to a local lesion but occurs in many cases whatever the site of origin of the toxins It is present in cases of both faucial and extra faucial diphtheria and is the local effect of exotoxin accepted from the general blood stream

The third or *generalised* form of diphtheritic paralysis is multiple neuritis It follows extra faucial as well as faucial diphtheria, and is also a result of the action of exotoxin circulating in the blood

As faucial diphtheria is the commonest form the most frequent nervous symptom is *paralysis of the soft palate* It is shown by the nasal quality of the voice and by the regurgitation of fluids through the nose As a rule the weakness is bilateral and equal but in some cases it is greater on the side on which the local lesion is more severe It makes its appearance in most instances about the end of the second week but may come on as early as the fourth day and as late as the sixth week The soft palate is relaxed and its movement on phonation is diminished The palate may be insensitive and its reflex is often diminished or lost Recovery usually occurs in a few weeks In rare instances the muscles of the pharynx and the vocal cords are paralysed Together with palatal palsy it is common to find marked weakness and tenderness of the sternomastoid muscles and masseters These are also local effects

Paralysis of accommodation appears about the same time as the palatal palsy perhaps a few days sooner The reaction of the pupils to accommodation as well as to light can almost always be obtained The trouble is subjective and is shown by defects of near vision—for example by inability to read small print Hypermetropes suffer great inconvenience In myopes it may pass unnoticed Paralysis of any of the extrinsic ocular muscles with strabismus and diplopia may occur and this may be either nuclear or peripheral in type

Multiple neuritis usually comes on 3 to 6 weeks after recovery from the throat infection Its presence is often detected when patients begin to exert themselves during convalescence Weakness and aching pains in the legs unsteadiness in walking clumsiness in performing fine movements with the hands feelings of pins and needles in the extremities—all these are common early symptoms Weakness affects in varying degree the muscles of the neck trunk and limbs It is generally slight in degree greater in the lower than in the upper extremities and greater in the extensor muscles than in the flexors Marked local atrophy is uncommon In severe cases life may be endangered by paralysis of the intercostals and of the diaphragm but fortunately one set of muscles has usually begun to recover before the other is seriously affected The small muscles of the hands and feet and the muscles of the calves and forearms are almost always tender on pressure They are soft and flabby and often show a partial reaction of degeneration

Sensory ataxy is almost always present and is often severe when the paralysis is trivial It causes the patient great inconvenience as it interferes seriously with walking and with the finer movements of the hands Objective examination reveals sensory impairment of the glove and stocking type On the hands and feet the loss to light tactile stimuli is often complete pain and temperature being less affected As the limb is ascended sensation gradually becomes normal Even when the sensibility of the skin is but little diminished the sensations of position and of passive movement in the extremities are often seriously impaired and the sense of vibration is often lost

In the early stages and for a few days the tendon jerks are exaggerated but are lost later in every case Their return is often long delayed, and it is common to see

patients months after recovery of normal power, in whom the knee jerks are still absent It is common also to find them absent many months after an attack of diphtheria in patients who give no history of nervous symptoms during the attack The skin reflexes are usually retained and stimulation of the sole gives a normal response

Cardiac failure is a grave but uncommon complication It is of myocardial origin Vasomotor paralyses and disturbances in the nutrition of the skin which occur so often in other forms of peripheral neuritis are never seen in diphtheria In those that survive the attack complete recovery from the nervous troubles always occurs

ACUTE FEBRILE POLYNEURITIS

Synonym —Acute Infective Polyneuritis

At various times small epidemics of a form of polyneuritis characterised by a febrile onset and by the involvement of the facial nerves have been described (Osler, Gordon Holmes, Rose Bradford and others)

Nothing is known of its ætiology and it is probably not essentially different from Landry's paralysis in nature though less fulminating in onset and not so liable to grave involvement of the trunk muscles

The onset is with slight fever, headache and malaise, pains in back and limbs, and such general symptoms as a coryza or gastro intestinal irritation The fever persists for 2 or 3 days only A few days then elapse before the signs and symptoms of polyneuritis develop It is said that the proximal limb muscles are more severely involved than the distal muscles a point of distinction from other forms of poly neuritis but this relative incidence of weakness is not invariable and has probably been over stressed The trunk muscles do not escape, and the face is often bilaterally paralysed As in other forms the paralysis is of the lower motor neurone type flaccid atrophic and with loss of tendon jerks Sensory loss is very slight, and there is rela tively slight muscular tenderness The cerebrospinal fluid may show a high rise in the protein content but is otherwise normal

The clinical course is variable, and sometimes fluctuating in the individual case Death may ensue from paralysis of the respiratory muscles, but recovery in the majority of cases is fairly rapid There is the usual tachycardia of polyneuritis If the patient survives the acute phase complete recovery ensues

DIABETIC NEURITIS

In many patients with glycosuria symptoms are present which point to changes in the peripheral nerves In some cases the only symptom is neuralgic pain in the distribution of one or more nerves This is commonest in the lower limbs where it simulates sciatica and sugar is found in the urine in the absence of any other sign of diabetes In other cases a single large nerve trunk suddenly becomes paralysed

In severe diabetes the knee jerks and ankle jerks are diminished or lost in more than half the cases This may accompany subjective sensory troubles in the lower limbs or it may appear as an isolated symptom The muscles are very often tender and the vibration sense of the feet is frequently absent To objective examination the sensibility of the skin is usually intact Perforating ulcers of the feet have been observed Only in very rare instances does the neuritis proceed to the stage of general ised peripheral paralysis of motor and sensory structures

PROGRESSIVE HYPERTROPHIC POLYNEURITIS

Dejerine and Sottas described an extremely rare progressive form of polyneuritis sometimes developing in infancy showing an heredo familial incidence and char acterised by thickening of the nerve trunks due to hypertrophy of the sheaths of

Schwann In recent years other cases of hypertrophic polyneuritis have been described which have no hereditary or familial character There is evidence that some at least of the cases described under this heading were examples of primary amyloidosis of the peripheral nervous system

Pathology —The thickening of the nerves may be palpable during life but is not invariably so Microscopically this thickening is found to be due to masses of non nucleated tissue arising from the sheath of Schwann

Symptoms —The malady develops and progresses very slowly with peripheral weakness muscular wasting sensory loss, loss of tendon jerks There may be noted in addition kyphoscoliosis, nystagmus and ataxy of movement It was formerly thought that the Argyll Robertson pupil was an integral part of the symptom complex but this is not the case

Prognosis —Death ultimately ensues from intercurrent disease

Treatment —There is no known treatment which is effective

LEAD PALSY

The nervous effects of lead poisoning are confined almost entirely to motor neurones Subjective sensory disturbances are often slight or absent and in most instances there is no objective sensory loss

Pathology —Aub in 1923 showed that the first event was the local concentration of lead in those muscles which were about to be paralysed and that the paralysis was a muscular event primarily and that secondarily the lead ascends along the motor axons and may finally cause the death of the ventral horn cell The degenerative changes in the nerves are confined almost entirely to the motor fibres and are most intense in the intramuscular twigs supplying muscles of the extensor groups Normal and degenerated fibres are found side by side the former becoming more numerous as the nerve is traced upwards Degenerative changes due to the action of lead are also found in the affected muscles

Symptoms —In most cases of the common *antebrachial* or *wrist drop type*, paralysis is limited to the extensor muscles of the fingers and wrists—that is to the muscles supplied by the musculo spiral nerve But the brachio radialis and the abductor longus pollicis also supplied by this nerve usually escape Inability to extend the first phalanges of the two middle fingers owing to weakness of the common extensor is usually the first difficulty The special extensors of the index and little fingers the long extensors of the thumb and the extensors of the wrist are next attacked and the characteristic wrist drop appears As a rule the paralysis becomes severe about a week after it is first noticed By this time it is usually bilateral and symmetrical but for several days or even for several weeks it may be confined to one side The affected muscles waste rapidly and the back of the forearm becomes flattened thus rendering the intact brachio radialis more prominent In this form loss of power always precedes atrophy and some muscles may show weakness without any wasting Recovery is almost always complete Simple weakness without atrophy usually passes off in a few weeks If the wasting is moderate and the muscles still react to faradism recovery may be expected in a few months When the atrophy is severe a year or more may elapse before recovery is complete

Occasionally the deltoid biceps brachialis and brachio radialis muscles are affected either alone or in company with the forearm muscles—*upper arm* or *brachial type* Less often paralysis occurs in the legs the muscles supplied by the peroneal nerve namely the long extensors of the toes and the peronei being chiefly involved—*peroneal type* Like the brachio radialis in the arm the tibialis anterior although supplied by the peroneal nerve usually escapes This type is usually associated with paralysis of the forearm muscles and runs the same course

In the form of paralysis described above the features are similar to those of a traumatic lesion to a nerve Loss of power precedes, and may be more extensive than wasting faradic irritability of the muscles is lost or diminished while the reaction to galvanism is retained and recovery is usually complete It is therefore called the degenerative form In the second form, the paralysis has the characters of progressive muscular atrophy Weakness and wasting come on together faradic and galvanic irritability of the muscles are both diminished in proportion to the wasting and the paralysis is often permanent This is known as the primary atrophic form. It occurs especially in the small muscles of the hand—*Aran Duchenne type*—but is sometimes irregular in its distribution and affects many muscles in all four limbs It is often associated with the first form but may occur alone Wasting comes on slowly and accompanies the loss of power, instead of succeeding it It is much more intractable than the degenerative form and often persists after muscles showing the first form of paralysis have recovered (See also Lead Encephalopathy p 368)

LANDRY'S PARALYSIS

In the year 1859 Landry applied the name acute ascending paralysis" to a case in which acute flaccid paralysis with loss of reflexes and without sensory disturbances commenced in the periphery of the lower limbs and rapidly spread upwards The arms were next involved, first in the periphery and later the trunk, respiratory muscles neck and lastly the cranial muscles were involved and death occurred from respiratory failure He made a careful microscopic examination of the spinal cord with the methods then at his disposal and failed to detect in it any morbid changes He subsequently described this symptom complex, which has since borne his name from an analysis of ten cases

Since this time a large number of cases have been recorded which from the acute nature of the onset and from the spreading nature of the paralysis have been described as cases of Landry s paralysis This name should be restricted to those cases of acute spreading paralysis in which disorders of sensibility and sphincter trouble are absent or little marked and in which recovery is complete if the patient survives and in which no gross lesion is found within the nervous system after death

Acute poliomyelitis may also in rare cases give rise to a spreading paralysis and cause much difficulty in diagnosis but it is invariable that some permanent paralysis remains upon recovery and further, the lesions of poliomyelitis are both gross and characteristic

Ætiology—What is known of the causation of the disease in general resembles very closely that of acute polyneuritis It affects males much more frequently than females and occurs chiefly in adult life between the ages of 16 and 54 years

Pathology—Slight hyperæmia of the spinal cord and especially of the grey matter with a few punctiform hæmorrhages is the only change noticeable upon naked eye examination Very definite histological changes are found upon microscopic examination in the anterior horn cells and in the cells of Clarke s column, where any degree of change may be found from an early pericentral chromatolysis to a complete loss of the chromatin granules and concentration of nuclei

The cerebrospinal fluid is clear It may present no abnormality either as regards cell or albumin content In other cases there is an excess of albumin and in this respect it resembles the cerebrospinal fluid of polyneuritis which is usually albuminous and sometimes so highly so as to clot spontaneously In a few instances the fluid contains numerous lymphocytes

Symptoms—The onset is in some cases abrupt, with the appearance of the characteristic spreading paralysis Much more frequently the paralysis is preceded by certain premonitory symptoms which may last from a few hours to days or weeks

These symptoms may consist in malaise headache lassitude insomnia anorexia constipation gastralgia vomiting and diarrhœa and there is not infrequently slight elevation of temperature More characteristic still among the prodromal signs are subjective disturbances of sensibility Pains in the back and limbs are common and may be of a dull aching nature or they may be sharp and shooting in character Numbness tingling 'pins and needles' and other paræsthesias may occur over any part of the body and are most commonly complained of in the periphery of the limbs The muscles may be locally tender during this prodromal stage

It is not uncommon for the paralysis to commence in the periphery of the lower extremities to ascend rapidly and to involve the muscles in the order of their innervation from the spinal cord the trunk becoming affected before the upper extremities and the intercostal muscles before the diaphragm The muscular weakness may commence in any group of muscles, as for example in the face neck upper extremities or trunk and when so commencing the spread of the paralysis is downwards constituting a descending type of paralysis

In Landry s paralysis as in acute polyneuritis the innervation of the respiratory muscles seems to be peculiarly resistant to the toxin

In those cases which recover the advance of the paralysis ceases and those muscles which have been most recently affected begin to show some recovery quickly

When the disease does not prove fatal either from respiratory failure pulmonary complications or sudden syncope the paralysis ceases to spread and the patient enters upon the stage of recovery

The paræsthesiæ which have been described with the onset often persist and there may be cramp like pains Not uncommonly the muscles are tender upon deep pressure but there is never that severe degree of tenderness met with in some forms of peripheral neuritis as for example in alcoholic neuritis There is exceptionally blunting of sensibility, most marked in the periphery, but this is never deep and is rapidly transient

Though from the general weakness of the trunk muscles there may be some difficulty in emptying the bladder and rectum during the first few days, and even retention with overflow incontinence that may require catheterisation from the same cause yet these last but a few days The deep and superficial reflexes disappear early with the onset of the first signs of the paralysis in the affected regions The psychic functions remain unimpaired throughout

Diagnosis—The rapidly spreading character of the paralysis in Landry s disease is so striking as to necessitate distinction only from those few maladies in which a similar rapidly spreading paralysis may occur and these are acute spreading myelitis intrathecal hæmorrhage acute poliomyelitis (spreading type) and acute polyneuritis Acute spreading myelitis is at once distinguished from Landry s paralysis by the severe sensory loss and sphincter paralysis which in the former condition develop *pari passu* with the motor paralysis and further if the myelitis does not involve the lumbo sacral enlargement of the spinal cord an extensor plantar reflex will be observed

The rare spreading form of poliomyelitis presents difficulty in diagnosis especially in the acute stage The general symptoms and the pyrexia are apt to be more severe in poliomyelitis An onset in childhood is more suggestive of poliomyelitis than of Landry s paralysis A fairly high polymorphonuclear leucocytosis in the blood and a lymphocytosis in the cerebrospinal fluid are in favour of poliomyelitis The persistence of local atrophic palsy on convalescence is absolute evidence of poliomyelitis The distinction of Landry s paralysis from acute febrile polyneuritis depends on the mode of spread of the paralysis and on the possible presence of numerous cells in the cerebrospinal fluid

Prognosis—In about one half of the cases the paralysis advances until the respiratory and bulbar muscles are involved and death occurs from respiratory failure usually on the third or fourth day but sometimes not until 10 days or more have

elapsed So long as the paralysis is extending and especially when the respiratory and bulbar muscles are failing the prognosis is very grave The extension of the paralysis may however cease at any stage, and when this occurs the prognosis at once becomes favourable even though there be considerable involvement of the respiratory and bulbar muscles

Treatment—The patient must be placed at complete rest and the discomfort and panic which are likely to arise from the utter inability to move must be assiduously relieved by frequent changes of posture The greatest care must be taken that the patient is adequately fed with nutritious and light food Stimulants are usually indicated A mercurial aperient should be administered early and the bowels regularly relieved for in some cases obstinate constipation occurs The bladder should be catheterised, if there is difficulty in micturition Both pain and pyrexia may be relieved by the administration of salicylates or aspirin

Atropine tends to check accumulation of secretion within the bronchi Oxygen may be administered where cyanosis occurs and it may be necessary to place the patient in a Drinker respirator When once there are signs that the malady has passed its height and that recovery is commencing little treatment is required except careful nursing and feeding Gentle massage may then be employed

MUSCULAR DISEASES

PRIMARY MUSCULAR DYSTROPHIES

Synonym—The Myopathies

Under this heading a disease is described in which the voluntary muscles undergo primary degeneration independent of detectable disease in other parts To facilitate description a number of clinical types have been distinguished according to the age at which the disease appears to the group of muscles first attacked to the presence or absence of pseudo hypertrophy and to the prominence of the hereditary factor The chief of these are—(1) the pseudo hypertrophic type (2) the juvenile type of Erb (3) the facio scapulo humeral type of Landouzy and Dejerine (4) the distal type

The first type is fairly constant but there is in reality no sharp division between the different forms That the others do not represent separate diseases is proved by the appearance of more than one of them in members of the same family The disease is familial and it is also hereditary in the sense that it may appear in some or all the members of a family through several generations

The changes in the muscles in the myopathies are essentially the same as those which occur when muscles degenerate from any other cause namely a slow and progressive atrophy of the contractile elements with a concurrent increase of fat and fibrous tissue However in most cases of myopathy swelling or hypertrophy of some of the muscle fibres is a feature of the microscopic picture and this hypertrophy is believed to represent an early stage of the degenerative process In the pseudo hypertrophic form the connective tissue hyperplasia is excessive in some of the affected muscles and their bulk is increased In the other forms of the disease and in those muscles in the pseudo hypertrophic form which become weak without any increase in size the overgrowth of connective tissue may balance the loss of bulk due to atrophy of the contractile tissues and the diseased muscles retain their normal size or atrophy may proceed faster than hyperplasia and the muscles waste from the beginning

1 PSEUDO-HYPERTROPHIC MUSCULAR DYSTROPHY

Ætiology—The cause of the disease is unknown In many instances no antecedent cases can be traced in the family In others a family history is obtained

always on the mother s side Isolated cases occur but more often several children are attacked in each generation Boys suffer more frequently than girls in a propor tion of about 5 to 1 Sometimes one sex alone suffers sometimes both It is rare for all the children to be attacked The males who escape beget healthy children whilst the females who appear to have escaped may transmit the disease to some of their offspring

Symptoms —The symptoms appear in early childhood The onset is often delayed to the fourth or fifth year rarely until towards puberty and very rarely until as late as the twentieth year In cases of late onset enlargement of the calves has usually been present for many years Weakness appears first in the muscles of the pelvic girdle The child who usually looks fat and strong begins to walk late he falls easily and rises again with difficulty He does not romp as other children do He cannot skip or jump and he has great difficulty in mounting stairs At first the muscles may be normal in size but as a rule some show obvious enlargement before the fifth year is reached The enlargement is most conspicuous in the calves the buttocks and the infraspinati The erector spinæ the quadriceps in whole or part the deltoid the supraspinatus and the triceps often show considerable hypertrophy Occasionally the masseters are enlarged At the same time other groups of muscles atrophy This is most severe and most frequent in the latissimus dorsi and in the lower part of the pectoralis major Later it extends to other muscles and ultimately to those which were at first hypertrophied The neck and face are spared There is no exact correlation between the size of the diseased muscles and their power but weakness is usually greatest in those which show most atrophy The defects are greater in the proximal muscles and diminish distally The hands often retain good power to the end This distribution of paralysis gives rise to certain character istic defects of attitude and movement.

In standing the legs are placed far apart and the upper part of the trunk is thrown back so that a plumb line from the most prominent vertebra falls behind the sacrum This attitude compensates for the forward tilting of the pelvis resulting from weakness of the glutei which normally raise the anterior border of the pelvis by lowering its posterior border In the sitting posture the lordosis disappears for now the attach ments of the flexors of the hip are approximated and these muscles no longer lower the anterior border of the pelvis On lying down the lordosis appears again, but can be abolished by relaxing the flexors of the hip joint, that is by flexing the hips passively In walking the feet are widely separated and to clear the ground with the advancing foot the body is inclined first to one side and then to the other This waddling produces a gait like that seen in congenital dislocation of the hip The early preponderance of weakness in the extensors of the hip and knee is betrayed by the great difficulty experienced in mounting stairs

The manner in which the child rises from the supine to the erect position is almost pathognomonic of the disease He first tries to sit up but fails He then rolls over on his belly and raises himself first on his knees and elbows and then on his hands and feet Next he places his hands on his knees and as it is impossible for him to raise the trunk actively owing to weakness of the extensors of the hip he literally climbs up his thighs Pushing the extensors may be enough to enable him to complete the movement if not he jerks the shoulders back suddenly and gains the erect posture by a writhing movement whose details are difficult to follow To climb the thighs successfully a certain amount of power is necessary to hold the knees slightly flexed When this power is lost he is no longer able to rise The arms are also used to assist the weak legs in sitting down and in getting up from a chair

As time goes on the weakness increases and invades all the muscles of the trunk and limbs Some of the muscles become shortened and distortions are produced by permanent alterations in the position of the joints The knees and elbows become

flexed, the feet take up the attitude of *talipes equinus* the spine becomes curved and the whole body is grossly deformed

The deep reflexes and the electrical excitability of the muscles diminish gradually as the wasting increases Sensation is unaffected The sphincters are not involved. The mental condition shows no abnormality

Diagnosis —The diagnosis is usually simple if a few of the outstanding features of the disease are known The defects of attitude and movement especially the mode of rising from the supine position, together with the characteristic association of enlargement of the infraspinati and calves with atrophy of the latissimus dorsi, form an unmistakable combination

Prognosis —This is most grave Few patients reach adult life, and most die within 10 years of the onset of the disease

Treatment —Drugs have no beneficial influence Glycine in large doses has been advocated but there is no reliable evidence that it affects the course of the disease Massage and passive movement are useful in the prevention of contractures and the efficiency of the muscles may be prolonged by suitable exercises Walking should be practised daily until it becomes impossible Very often this is lost owing to contractions of the calf muscles and is regained after tenotomy

2 OTHER TYPES OF MUSCULAR DYSTROPHY

Ætiology —The separation of the remaining types of myopathy from the pseudo hypertrophic form is not an absolute one, as isolated cases are occasionally met with which seem to form a connecting link between the several varieties The varieties however are habitually separate in occurrence and in families in which numerous cases conforming to the types to be described hereunder have occurred throughout several generations no cases presented the peculiar features of the pseudo hyper trophic form Moreover the sex incidence as well as the period of onset is different in the two varieties and it is possible that there is some essential pathological difference between them and that they are separate diseases With regard to the types of myopathy unassociated with pseudo hypertrophy no doubt exists as to their fundamental unity They are merely varieties of one disease

The influence of heredity is much more prominent than in the pseudo hypertrophic form Isolated cases occur, but they are rare In most instances several members of a family are affected in the same and in succeeding generations

The sexes suffer equally The time of onset varies within wide limits—from infancy to old age When the wasting begins in the face (*facio scapulo humeral type*) the disease frequently begins in childhood but sometimes it begins there late in life In the cases where it is first noticed in the muscles of the shoulder and pelvic girdle the onset is most frequent between the ages of 15 and 35 (*Erb s juvenile type*) but here again it may begin in childhood or early old age and the term juvenile is hardly applicable to it The same variations in the age of onset are noticeable in cases where the atrophy begins in the forearms and legs (*distal type*)

The various types may be exemplified in members of the same family and in the same family the age of onset may show extreme variation

The cause of the disease is quite unknown

Symptoms —In the so called juvenile form weakness and wasting come on simultaneously In most cases they are first noticed in the arms but in some families the legs suffer first Of the arm muscles the biceps triceps and brachio radialis are most often first affected The lower part of the pectoralis major the latissimus dorsi trapezius and rhomboids are attacked in most cases Atrophy of the serratus magnus is common, but it may escape even in severe cases The deltoid supra spinatus infraspinatus and subscapularis usually escape Atrophy of the forearm and hand muscles is rare

In the legs, the flexors of the hip the extensors of the knee and the glutei are most frequently affected The muscles below the knee often escape entirely

In the face the zygomatic muscles and the orbiculàris are attacked The face is dull and expressionless the naso labial fold is obliterated the lips are habitually separated and the lower lip projects—myopathic facies The face does not light up in conversation in blinking the eyes are incompletely closed and the articulation of labial consonants is defective In smiling the mouth forms a straight line instead of its angles being drawn upwards and outwards by the zygomatici The power of whistling is lost When the patient closes his eyes or compresses his lips as forcibly as he can they can be forced open with great ease The buccinators are often affected the tongue and the masticatory muscles never The spinal muscles often atrophy and in a few cases the abdominal muscles have been involved The excitability of the muscles to faradic and galvanic stimulation usually diminishes in proportion to the wasting The muscles never show fibrillary tremors Sensibility is unaffected and all the other functions of the nervous system are normal Deformities are neither so common nor so severe as in the pseudo hypertrophic form

Diagnosis —In isolated cases the diagnosis of myopathy from spinal progressive muscular atrophy is based upon the distribution of the wasting upon the disproportionate weakness and the absence of fibrillation in the affected muscles and the age of the patient When a family history of atrophy is obtained dystrophia myotonica and peroneal muscular atrophy must be excluded Dystrophia myotonica is distinguished by the peculiar prolonged response of some of the muscles to voluntary electrical and mechanical stimulation and by the distribution of the wasting Atrophy of the sterno mastoids which is constant and severe in dystrophia myotonica is never seen in the forms of myopathy now under consideration In peroneal muscular atrophy the combination of atrophy in the lower limbs and small muscles of the hands together with sensory disturbances in the lower limbs is distinctive In an early case when the hand muscles are still normal and sensory changes are absent the differentiation from myopathy may be impossible for a time

Prognosis —The disease shows wide variations in its course and duration The atrophy may remain confined to the group of muscles in which it begins or extension may take place after an interval of several years It rarely extends beyond the muscles mentioned above In most cases even in those that begin in childhood progress is extremely slow and as no symptom of the disease is necessarily fatal death usually results from other maladies unconnected with the disease

Treatment —Owing to the variable course of the disease it is impossible to estimate the value of any treatment that may be employed Massage and especially voluntary exercises designed to bring the weakened muscles into play seem sometimes to retard the progress of the disease

AMYOTONIA CONGENITA

Synonyms —Oppenheim s Disease Myotonia Congenita

Definition —A malady of early childhood usually congenital and sometimes familial characterised by extreme flaccidity smallness and weakness of the muscles which are not actually paralysed by lowering of the faradic excitability of the muscles by loss of the tendon jerks and by contractures in the region affected

Ætiology —In most cases the disease is present at the time of birth in a few cases it has appeared during the first year of life in an apparently healthy child and sometimes following an acute illness such as bronchitis or diarrhœa Usually sporadic, it has occurred in several children of the same parents Some authorities consider that it is a variant of the Werdnig Hoffmann disease (*q v*) (p 1565)

Pathology —The chief morbid changes are found in the muscles In these very

conspicuous pathological conditions are present, closely resembling those found in the myopathies The three most striking conditions are—(1) the minute size of the majority of the muscle fibres from 7μ to 12μ (2) the presence of a few very large or giant " fibres reaching 140μ in diameter, and larger than any fibre occurring in normal muscle, (3) marked regressive changes in the giant fibres There is increase of the connective tissue between the muscle bundles Reduction in numbers of the ventral horn cells of the spinal cord occurs and the ventral roots are small and poorly myelinated

Symptoms—The extreme flaccidity of the affected muscles is noticed from the time of birth They are small and weak, and though there is no muscular wasting and no absolute paralysis, yet in many cases the limbs cannot be raised against the action of gravity, nor can the head be held up The great relaxation of the muscles and ligaments allows of the most fantastic attitudes being assumed without pain When the child gets older, he is unable to sit up but when placed in the sitting position the spine bunches up from absence of any muscular support and he is unable to support his weight upon the weak legs The amyotonia is symmetrical and affects the legs always the trunk often the arms not infrequently but never the face Notwithstanding the flaccidity some degree of flexor contracture is usually present The faradic excitability of the muscles is much lowered but not lost Sensibility and the sphincters are not affected The superficial reflexes are normal but the deep reflexes are invariably absent in the affected regions The children are usually intelligent with good bodily development and growth proceeds normally

Diagnosis—This presents no difficulty on account of the presence of the flaccidity at birth the absence of the deep reflexes and the tendency slowly to improve It has to be separated from those maladies to which it bears a superficial resemblance namely the myopathies rickety weakness, obstetrical infantile and diphtherial palsies

Course and Prognosis—Some of the children succumb during the early and severe stages of the disease but the tendency of the disease is to improve slowly in the course of years and in some cases almost complete recovery with return of the knee jerks occurs

Treatment—This consists in aiding the natural tendency to improve with massage passive movements and exercises in treating contractures with tenotomy and in attending to the general health and nutrition

DYSTROPHIA MYOTONICA

Synonym—Myotonia Atrophica

Definition—A disease of familial incidence which begins usually in the third and fourth decades of life and which is characterised by muscular atrophy of peculiar distribution and unlike that of any other disease This atrophy occurs first and most in the sterno mastoids and facial muscles next in the muscles of the forearms and may also be found in the muscles of mastication in the vasti and in the dorsiflexors of the feet and peronei Associated with this wasting but not commensurate with it nor necessarily occurring in the same muscles is a peculiar difficulty in relaxing the muscles after effort called myotonia which gives to this malady an especial feature which at once separates it from all other forms of muscular atrophy Signs of bodily dyscrasia are often present the most important of which are cataract premature baldness atrophy of testicles loss of sexual power and general bodily wasting This disease was first placed upon a firm clinical basis by Batten and Gibb and Steinert in 1909 Curschmann in 1912 adopted the term Dystrophia Myotonica as being more correctly descriptive

Ætiology—This condition is probably always familial and the heredity is homologous—that is it tends to appear in the same child rank in a number of

apparently unconnected families at a common distance from one and the same ancestor and often it seems to be entirely confined to one child rank The descent of the latent tendency is equally through the males and females but the males more frequently transmit The presence of the heredo familial disease in earlier generations is often betrayed by other signs such as cataract frequent celibacy childless marriages high infant mortality and a dying out of certain branches of the family The malady has been observed at the age of 10 years but usually the onset occurs between the ages of 20 and 35 years A large number of the patients have been unusually gifted and proficient in athletics prior to the onset Both sexes may be affected No exciting causal factors are known

Pathology —No definite changes have been found in the nervous system The muscles presenting the myotonia have repeatedly been examined and found normal In the atrophic muscles the morbid process singles out certain fibres especially so that thick and thin fibres are found lying together There is increase of the muscle nuclei round thick and thin fibres alike though some atrophic fibres may be found with no increase of nuclei Recent biochemical and electrographic studies by Brown and Harvey of a form of congenital myotonia in goats suggest that there is no functional disorder of neuromuscular transmission of the motor impulse but that the disorder is in the muscles themselves

Symptoms —The onset is gradual and the course extremely slow The first symptom to call attention may be either the difficulty in relaxing after muscular effort—the clinging of the hand to the tool which has been grasped the smile that is so slow to disappear—or the weakness and wasting of the muscles The two chief signs of the disease—the myotonia and the wasting—seem to have no connection the one with the other either as regards coincidence in time or place The myotonia may appear years before there is any obvious wasting Moreover the muscles which show the most conspicuous myotonia are often those which are not wasted and finally those muscles which waste greatly tend to lose any sign of myotonia which they may have had The extent and the intensity of the muscular atrophy and of the myotonia show great variations The atrophy may be widely spread and many muscles may be myotonic or the former may be severe and the myotonia slight or both may be present in minor degree only Lastly there are cases in which only the atrophy or only the myotonia is present The myotonia consists in an inability to relax a muscle immediately after it has been put into voluntary contraction and the greater the effort used in contracting the muscle the greater the difficulty with relaxation The patient grasps one by the hand and is unable to disengage the hand but pulls it away still grasping and it may take seconds to relax He smiles quickly to a suitable stimulus and the face remains fixed at the height of the smile for long after the emotion has vanished In eating his jaw becomes fixed he is unable to perform alternating movements in the muscles which are affected except at a very slow rate When the myotonia is severe and general he is liable to fall like a log when walking from inability to relax muscles which have been put into contraction The myotonia is seen most often and to a greater extent in the flexor muscles of the forearm and in those of the face but it may be quite general In the same patient it may be very marked at one time and absent at another The muscular weakness and wasting usually have a most typical distribution involving the sternomastoids and other muscles of the neck the facial and masticatory muscles—giving rise to the sad myopathic face the vasti of the thighs the dorsiflexors of the feet and the flexor muscles of the forearms and this is the usual order in which the muscles are affected It is always in one or other of these groups that the wasting commences but sometimes the sequence of muscles attacked is quite different Fibrillation does not accompany the atrophy The electrical reactions show a reduction both to faradic and to galvanic stimuli with a tendency to a polar change The myotonic reaction consists in a very long lasting contraction when the muscles are stimulated with every

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Ætiology —This condition is probably always familial and the heredity is homologous—that is it tends to appear in the same child rank in a number of

Ætiology—Beyond the facts that the malady is usually hereditary and familial only a few sporadic cases occurring and its incidence in early childhood nothing is known of the causes Cold heat fatigue and hunger conspicuously increase the symptoms

Pathology—The affected muscles are actually hypertrophied and are always *firmer to the feel than normal muscles while sometimes they show a board like hard*ness The individual fibres show considerable hypertrophy

Symptoms—The presence of the disease first becomes evident from slowness clumsiness and awkwardness of movement with a great tendency to fall if the balance is upset This is often most noticeable after rest when on attempting to move the limbs seem glued down and move very slowly Often the patient is able with exercise to work the stiffness off and the myotonia lessens in the muscles which are being used but if he is suddenly called upon to put another set of muscles into action as for example by losing his balance he is at once caught up by the myotonia and so is apt to fall In other cases the myotonia increases or is uninfluenced by exertion The muscles of the legs are as a rule most affected but sometimes all the muscles of the body may be involved

Passive movement does not reveal the presence of any rigidity The abnormality affects only the relaxation of the muscles after voluntary contraction the peculiar feature being the slowness of relaxation due to the continuance of the contraction of the muscle fibres for a variable number of seconds after voluntary impulses have ceased The peculiarities of electrical excitability bear the name of the myotonic reaction of Erb The contraction either on faradic or galvanic stimulation lasts much longer than the normal and relaxes very slowly and this is more marked the stronger the current used with the application of galvanism slow wave like contractions of the muscle are seen to proceed slowly from the cathode to the anode There is no pain no sensory disturbances or loss and the sphincters and reflexes are unaffected

Diagnosis—The only malady which can be confused with Thomsen s disease is dystrophia myotonica in which the myotonic symptoms and signs are identical In the latter malady the onset is at a much later age the incidence of the spasm is upon local groups of muscles and the characteristic weakness of the facial muscles and atrophy of the sternomastoids etc at once distinguish it

Course and Prognosis—Thomsen s disease has no tendency to shorten and destroy life It tends to become more marked from infancy to puberty and then less marked again as age increases It has never been known to recover spontaneously

Treatment—No cure for the disease is at present known The administration of quinine hydrochloride in doses of gr 10 to gr 15 by mouth t d s may give considerable symptomatic relief Conditions which increase the myotonia such as cold fatigue and hunger should be avoided Most patients are the better for regular exercise as was observed by Thomsen who was himself afflicted with the disease

MYASTHENIA GRAVIS

Definition—A chronic malady of adult life characterised by an excessive fatiguability of the voluntary muscles especially those innervated by the cranial nerves This leads to a variable paralysis of the muscles concerned which is brought on or rapidly increased by exertion and tends to improve with rest but which may ultimately become permanent

Ætiology—The malady seems to have become more prevalent in this country *during the past 30 years It affects predominantly* young adults between the ages of 20 and 30 It very rarely occurs before puberty but cases beginning in middle or late life are by no means as uncommon as was formerly supposed The sexes

form of stimulus and if the latter be strong it may last as long as 30 seconds This is usually present in the muscles which are myotonic and not wasted and some modification of it is often superadded to the other electrical changes in those muscles which are wasted

The affection of the muscles of the face and jaw entails some alteration of articulation and phonation The voice is low, it lacks intonation and has a definite nasal quality Sensibility is not affected

The rule is for the tendon jerks to be diminished or lost and it is very rare for all the jerks to be present in any case

Apart from symptoms and signs connected with the muscles the most important sign of the dystrophy is cataract which occurs in more than half of the cases This cataract is often met with in otherwise healthy brothers and sisters of those who have the muscular changes and in otherwise healthy members of earlier generations in the afflicted families In succeeding generations after its first appearance the age of occurrence of this cataract shows remarkable anticipation'—that is commencing at first as senile cataract it appears at an earlier and earlier age with each successive generation until with fully developed myotonia atrophica it appears in youth The presenile cataract of the dystrophic generation begins as small peripheral opacities first in the posterior and later in the anterior cortical lamellæ sometimes with fine point like opacities scattered through the lens It ripens quickly to a total soft cataract, with a small central nucleus

The genital organs remain infantile in some cases celibacy and childless marriages are common More often sexuality is normal until the onset of definite symptoms after which desire and power disappear, and ultimate atrophy of the testicles is usual Early frontal baldness is the rule A general wasting of all the tissues of the body is seen in many cases

Diagnosis—There is no difficulty in the diagnosis when the distribution of the muscular atrophy is typical and when myotonia is obvious it simply involves a recognition of the unique characteristics of the disease When the myotonia precedes the wasting the age of onset will distinguish this malady from Thomsen s disease myotonia congenita and the oncoming of any sign of facial weakness or muscular wasting will make the diagnosis certain When the myotonia does not appear until long after the wasting is apparent the diagnosis is much more difficult, but the wasting of the sternomastoids is characteristic

Course and Prognosis—This malady usually progresses very slowly but occasionally very extensive and incapacitating wasting of muscles and weakness may develop within a year of the first symptom Some cases seem to remain stationary for very long periods The tenure of life is certainly short in all cases and does not appear to be prolonged beyond the middle of the fifth decade The oldest patient reported in the records as still living was aged 50 years

Treatment—It has been found that the administration of quinine gr 10 to 15 daily lessens the myotonia considerably Neither electrical treatment nor massage has the slightest effect in altering the course of the disease

MYOTONIA CONGENITA

Synonym—Thomsen s Disease

Definition—A very rare malady commencing in early childhood which is hereditary and familial and characterised by a striking slowness in the relaxation of the muscle after voluntary effort On voluntary contraction the muscles pass into a spasm which relaxes very slowly resembling the contraction of the veratrinised frog s muscle and its subsequent slow relaxation Peculiar changes in the electrical excitability of the muscle and hypertrophy of the muscle fibres are constant

may give rise to so much fatigue of the masticatory muscles that only soft foods can be taken and towards the end of a meal the lower jaw may be too heavy for the exhausted muscles to sustain and the patient may be seen supporting it with the hand and attempting in this way to supplement the process of mastication The muscles of the face commonly share the weakness Friends observe that towards the end of the day the patient s face is expressionless or comment on the peculiar snarling quality of the smile The patient may complain that he cannot smoke a cigarette or whistle as the lips cannot maintain a sustained pressure In severe cases the eyelids can only be closed with difficulty and it may be noticed that the patient sleeps with the eyes open Fatigue of the neck muscles may be an early symptom The head feels more and more heavy and finally can only be supported with the aid of the hand The weakness may affect any or all of the muscles of the limbs and trunk though the arms are more frequently involved than the legs The soldier may find that after a few minutes rifle drill becomes impossible or the schoolmaster that after writing on the blackboard for a short time he is no longer able to support the weight of his arm Women may complain that they cannot keep their arms up long enough to do their hair Whatever the initial presenting symptom may be the extent of the disorder gradually spreads until a wide range of voluntary movements is affected

Few diseases present a more characteristic picture than does myasthenia gravis in its established stage The variable and usually asymmetric ptosis is seldom absent It can readily be brought on or increased by asking the patient to look upwards for a few seconds and when severe one or both eyes may be fully closed Unlike the ptosis of tabes there is little compensatory wrinkling of the forehead because the frontales share the weakness of the levatores palpebrarum The ocular palsies are characteristic any or all of the external ocular muscles may be involved and strabismus is common The paralyses rapidly increase in severity and extent with ocular movement and a few attempts to glance from side to side may bring all oculomotor activity to an end The pupils are always normal in their reactions The ocular more than any other muscles show a tendency to develop complete and unvarying *paralysis in long standing* cases and *with the exception of the extremely rare disorder* described as progressive nuclear ophthalmoplegia there is no disease other than myasthenia which gives rise to a complete external ophthalmoplegia with normal pupils in the absence of other signs of nervous disease Fortunately when the stage of permanent ophthalmoplegia is reached the optic axes are usually parallel and diplopia disappears

The facies of myasthenia with its lack of expression the inability to close or pucker the eyes or to wrinkle the forehead and the peculiar weak nasal smile is unmistakable Weakness of the muscles of palate pharynx and larynx may be general or localised and at first is present only after use Permanent paralysis of the soft palate is commonly seen in chronic cases that of the vocal cords or pharynx being much more rare Severe weakness of the tongue may be associated with some reduction in the size of the organ but with this rare exception wasting is not seen in myasthenic muscles nor are the tendon reflexes disturbed Sensibility and sphincter functions are unimpaired The excessive tendency to fatigue which is responsible for the symptoms of myasthenia is also seen in the muscles in their response to electrical stimulation With an interrupted faradic current the contraction of the muscles is at first normal but instead of remaining at a similar strength for an indefinite period it rapidly decreases until it disappears altogether If the stimulation is discontinued for a few minutes and then recommenced there is a further response which tires more readily than the first After exhaustion by faradism some volitional response remains

Diagnosis —This is seldom a matter of difficulty if the variable paralysis increasing with fatigue and improving with rest is conspicuous for this phenomenon

are equally affected Nothing is known of any causal factor, either immediate or *remote*, though the first onset of symptoms has not infrequently been noted after an acute infection particularly of the naso pharynx The one clinical association which cannot be ignored is with exophthalmic goitre for not only may myasthenia follow that disorder but the ocular palsies and muscular weakness which may occur in Graves' disease bear no small resemblance to those of myasthenia

Pathology—The only change found within the nervous system either central or peripheral is slight atrophy of those nerve cells which supply long paralysed muscles and these changes are certainly not primary Nor is there any essential histological change in the affected muscles except where long standing complete paralysis is associated with the degeneration of long disuse Small aggregations of lymphocytes, known as lymphorrhages have been described in the muscles in some cases

In a large proportion of the cases subjected to autopsy some degree of persistent thymus has been found This may vary between a well formed organ weighing several grammes and small remnants or thymic rests These thymic elements may show evidence of proliferation or degeneration

Chemical examination reveals no significant disturbance in the metabolism of glucose calcium phosphorus or creatinine although in common with most muscular disorders, creatinuria may be present in myasthenia There is evidence that the muscle potassium is increased and that it reverts to normal when the myasthenic symptoms are abolished by an injection of neostigmine

The view expressed in earlier editions of this book that the seat of the disorder of function responsible for myasthenia gravis is at the myo neural junction has of recent years received confirmation from observations made with physostigmine and the synthetic substance neostigmine (Prostigmin) It is believed that the normal transmission of impulses from the motor nerve fibres to the voluntary muscles through the motor nerve endings depends upon the liberation at the end plate of acetyl choline In myasthenia the failure of effective innervation may be due to the inadequate liberation of acetyl choline or to its premature or excessive destruction by choline esterase or to the presence of a curare like substance antagonistic in its action to acetyl choline The administration of physostigmine temporarily delays the destruction of acetyl choline by the choline esterase normally present in the blood and during the period of its activity renders muscular contraction normal The exact nature of the defect still awaits elucidation

Symptoms—The onset of the disorder is usually insidious but in rare cases may be acute The symptoms can all be related to excessive fatiguability of muscles and thus make their appearance after use and improve with rest and are most severe in the evening and least marked on first waking in the morning The muscles first affected are usually those innervated by the cranial nerves particularly the external ocular muscles but as the disease progresses the extent of the disorder spreads to involve the muscles of the neck limbs and trunk Sometimes however the characteristic weakness is universal from its commencement

Ocular symptoms are of the greatest importance The clerk finds that towards the end of the day he is seeing double or that one or both upper eyelids droop In the morning on waking the ptosis and diplopia have both disappeared only to return after another day's work The school teacher notices that as he lectures his voice gradually grows weaker and more husky and acquires a nasal quality This too clears up with a rest and is invariably worse towards the end of the day Difficulty in swallowing is a common symptom At the commencement of a meal all may be well but as it goes on the food is forced down with increasing difficulty until finally swallowing is no longer possible Many patients find that they can eat their solid meals only in the early part of the day and by evening can at best sip fluids Nasal regurgitation of fluids towards the end of the day is common. The act of chewing

may give rise to so much fatigue of the masticatory muscles that only soft foods can be taken and towards the end of a meal the lower jaw may be too heavy for the exhausted muscles to sustain and the patient may be seen supporting it with the hand and attempting in this way to supplement the process of mastication The muscles of the face commonly share the weakness Friends observe that towards the end of the day the patient s face is expressionless or comment on the peculiar snarling quality of the smile The patient may complain that he cannot smoke a cigarette or whistle as the lips cannot maintain a sustained pressure In severe cases the eyelids can only be closed with difficulty and it may be noticed that the patient sleeps with the eyes open Fatigue of the neck muscles may be an early symptom The head feels more and more heavy and finally can only be supported with the aid of the hand The weakness may affect any or all of the muscles of the limbs and trunk though the arms are more frequently involved than the legs The soldier may find that after a few minutes rifle drill becomes impossible or the schoolmaster that after writing on the blackboard for a short time he is no longer able to support the weight of his arm Women may complain that they cannot keep their arms up long enough to do their hair Whatever the initial presenting symptom may be the extent of the disorder gradually spreads until a wide range of voluntary movements is affected

Few diseases present a more characteristic picture than does myasthenia gravis in its established stage The variable and usually asymmetric ptosis is seldom absent It can readily be brought on or increased by asking the patient to look upwards for a few seconds and when severe one or both eyes may be fully closed Unlike the ptosis of tabes there is little compensatory wrinkling of the forehead because the frontales share the weakness of the levatores palpebrarum The ocular palsies are characteristic any or all of the external ocular muscles may be involved and strabismus is common The paralyses rapidly increase in severity and extent with ocular movement and a few attempts to glance from side to side may bring all oculomotor activity to an end The pupils are always normal in their reactions The ocular more than any other muscles show a tendency to develop complete and unvarying paralysis in long standing cases and with the exception of the extremely rare disorder described as progressive nuclear ophthalmoplegia there is no disease other than myasthenia which gives rise to a complete external ophthalmoplegia with normal pupils in the absence of other signs of nervous disease Fortunately when the stage of permanent ophthalmoplegia is reached the optic axes are usually parallel and diplopia disappears

The facies of myasthenia with its lack of expression the inability to close or pucker the eyes or to wrinkle the forehead and the peculiar weak nasal smile is unmistakable Weakness of the muscles of palate pharynx and larynx may be general or localised and at first is present only after use Permanent paralysis of the soft palate is commonly seen in chronic cases that of the vocal cords or pharynx being much more rare Severe weakness of the tongue may be associated with some reduction in the size of the organ but with this rare exception wasting is not seen in myasthenic muscles nor are the tendon reflexes disturbed Sensibility and sphincter functions are unimpaired The excessive tendency to fatigue which is responsible for the symptoms of myasthenia is also seen in the muscles in their response to electrical stimulation With an interrupted faradic current the contraction of the muscles is at first normal but instead of remaining at a similar strength for an indefinite period it rapidly decreases until it disappears altogether If the stimulation is discontinued for a few minutes and then recommenced there is a further response which tires more readily than the first After exhaustion by faradism some volitional response remains

Diagnosis —This is seldom a matter of difficulty if the variable paralysis increasing with fatigue and improving with rest is conspicuous for this phenomenon

occurs in no other disease Even so, in its early stages, the malady is often mistaken for a hysterical disturbance More legitimate difficulty may arise when only isolated and permanent paralysis is present, especially as such cases are liable to present themselves in ophthalmic or laryngological departments It should be remembered that any unilateral or bilateral palsy of muscles supplied by the cranial nerves may be myasthenic Here the history of slow onset with variable paralysis and fatigue phenomena, can nearly always be obtained and the absence of the usual signs of gross lesions of the brain stem nuclei or of progressive diseases affecting the latter, should avoid confusion When as sometimes happens, myasthenia begins with a unilateral ophthalmoplegia or laryngoplegia the diagnosis may be really difficult. The possibility of such should be borne in mind and a careful watch kept for the appearance of conclusive evidence An intramuscular injection of 1 ml of the standard solution of neostigmine may be used as a diagnostic test, its effect being to bring about within half an hour the temporary abolition or very great amelioration of any variable symptoms that are due to myasthenia gravis

Course and Prognosis—Although myasthenia gravis is invariably a dangerous disease as its name implies its course is extremely variable In some cases the degree of the muscular involvement steadily increases in extent and severity until a fatal outcome is reached in a few months or years In such cases death usually results from progressive respiratory failure or from aspiration broncho pneumonia consequent upon pharyngeal and laryngeal palsy supervening upon a state of inanition Not infrequently death is sudden and unexpected and appears to be due to syncope In other cases the disorder may remain confined for a long period to small groups of muscles particularly those of the eyes and may result in a condition of multiple cranial nerve palsies of an unvarying character with a survival period of 20 to 30 years In such cases more generalised and active symptoms may reassert themselves at any time and death may occur after many years of stability In yet a third group long periods of complete remission may occur ultimately followed by a recurrence of characteristic symptoms, which on this occasion may prove to be progressive

Treatment—The treatment of this disorder was revolutionised by the discovery of the specific effect of physostigmine and its synthetic relative neostigmine Few things in medicine are more dramatic than the sudden amelioration of symptoms the relief of ptosis the recovery of ocular movement and the return of facial expression that follows the administration of one of these drugs The effect is however, transitory lasting only from 4 to 6 hours and is in no sense curative It is usual to administer 2 to 4 ml of neostigmine (1 to 2 mg) subcutaneously two or three times daily half an hour before meals If the drug causes abdominal discomfort or palpitation it may be combined with atropine sulphate gr $\frac{1}{150}$ Alternatively the drug may be given by mouth in doses of 10 to 25 mg three or four times daily In severe cases the period during which the effect of the drug is wearing off may be attended by severe and alarming weakness and over a prolonged period the beneficial action of the drug tends to lessen and an increased dose is required to be effective The administration of ephedrine gr $\frac{1}{4}$ to 1 b d has been found beneficial it may be sufficient of itself to keep a mild case in reasonable comfort or it may be used as an adjunct to neostigmine

The frequent association of a persistent thymus with myasthenia has long received attention and has led to attempts to treat the disorder by influencing this organ Numerous isolated examples of improvement in symptoms following radiotherapy to the thymus are recorded in the literature but the results were not constant Of recent years a number of cases have been treated by surgical removal of the thymic remnants with encouraging results This operation is one which carries a considerable mortality and should only be attempted by an expert in thoracic surgery Of the patients who have been so treated some have shown a degree of improvement amounting to a cure and quite different from anything seen with neostigmine therapy

Others after a period of improvement have relapsed Others again have shown no material alteration in their condition The procedure should at present be regarded as an encouraging but not yet fully established advance in treatment

FAMILIAL PERIODIC PARALYSIS

Definition —A flaccid paralysis affecting the muscles of the trunk and of the extremities associated with loss of the deep reflexes and diminution or loss of faradic *excitability in the muscles The paralysis is temporary in character though it may* be fatal during the attack and it recurs at intervals It is a rare malady, some 200 cases having been reported in the literature

Ætiology —It has been noted as early as the fifth year and as late as the thirtieth year but usually it appears about the age of puberty Most of the cases occur in the male sex Heredity is very marked and the malady has been traced through five generations Transmission may occur either through the male or through the female and not infrequently a generation is skipped Several members of the same family are usually affected

Pathology —*Several cases have come to necropsy but no lesion which could be* associated with the symptoms was found Biopsy of the muscles has given entirely negative results During an attack significant fall in the serum potassium has been demonstrated An attack may be brought on by a large intake of glucose especially if an injection of insulin is given at the same time

Symptoms —The clinical picture is so striking as to be almost dramatic The patient retires to bed feeling perfectly well and awakens in the morning without pain or malaise but with a flaccid motor paralysis which always involves all four extremities and which may reach all the muscles of the body except those of the organs of speech deglutition and respiration and even these are often partially in volved Severe involvement of these vital muscles during an attack has caused death The bladder and rectal functions are retained and it is unusual for the patient either to void urine or fæces during the attack The paralysis is usually at its height on waking but it may subsequently increase After lasting for a variable time from a few hours to a few days it passes off sometimes gradually sometimes rapidly In one family it was astonishing how the patients on waking in an attack could judge invariably how long the particular attack would last They could judge with unfailing certainty when ability would return and were in the habit of arranging their business accordingly Most of the patients in addition to the severe attacks of paralysis suffer from what they call morning weakness temporary inability to grip with the hands and slight disability with the feet on waking The paralysis in periodic paralysis is flaccid and there is loss or marked diminution of response to faradism during the paralysis The deep and superficial reflexes are lost in the paralysed region Objective sensation is not affected but there may be subjective sensations of tingling and numbness and the muscles may be a little sore and stiff after the attack Flushing of the face and profuse sweating may occur during an attack There is an invariable tendency for the attacks to diminish in frequency and severity after middle life is reached

Diagnosis —This must be evident to any one acquainted with the symptoms of the disease

Treatment —Potassium chloride in large doses (up to gr 30 or 40) will avert or cut short an attack No other remedial measure is known

J Purdon Martin
J St C Elkington

SECTION XIX

PSYCHOLOGICAL MEDICINE

INTRODUCTION

Psychiatry is concerned with forms of illness as widespread and diverse as those of somatic medicine There are almost as many beds in mental hospitals colonies for defectives and allied institutions as in all other hospitals put together and there is an undoubtedly large, if unnumbered part of the population who have mild mental disorder not needing mental hospital care hysteria obsessional neurosis hypo chondria chronic depression paranoid states and so forth The diversity of this widespread group of illnesses depends on their being disorders of mind—disorders that is, of the human function which comprehends and sums up all other functions of the organism serves to relate a human being to his complex environment and is the chief token that he is an individual, and not a sample Mental disorders are therefore varied as are the people who suffer from them It is only by ignoring most of what is individual in these illnesses that a few common types or categories can be recognised, comparable to the diseases of somatic medicine Such a procedure is necessary for practical ends material must be classified Moreover a biological foundation may be assumed for the syndromes with which psychiatry works They stand for the main ways in which a human being can become mentally unhealthy There are only a few such ways and they are determined by the struc tural and functional patterns inherent in the organism Diversity arises through their becoming manifest under the influence of each individual s special environment and in combination with his other inherited tendencies Diversity therefore can be due to a combination of single hereditary causes and to the effect of each individual s environment throughout his life upon his development and behaviour There is always interplay between inheritance and environment Part of the psychiatrist s business is to discover how this interplay has led to the present illness The inter play moreover is sufficiently varied in the course of each patient s life to make prog nosis and the effect of treatment a matter of individual study rather than of summary inference from the diagnosis once made

Treatment is only another special instance of the environment acting on the patient its power and limitations for him cannot be judged without considering what effects this or that experience has had on his previous life Consequently the psychiatrist even more than the general physician must study illness in two ways first as showing some typical pattern of morbid behaviour with characteristic patho logical changes and tending to run along well known lines and secondly as a patch of personal biography something to be understood rather than classified in terms of psychology and physiology The two methods are complementary though in a brief textbook presentation the former must be the more prominent

There is no dividing line between somatic medicine and psychiatry Psychiatry although it has to work in part with social and psychological conceptions of which general medicine has hitherto felt less need suffers greatly when it limits itself to this way of regarding mental phenomena It cannot safely ignore the relationship between bodily happenings and the patient s state of mind Crude instances of this relationship are the delirium that accompanies an acute fever and the irritable fatigue (neurasthenia) that may follow it the insanity that is due to cerebral tumour or general paralysis of the insane the obsessional neurosis that follows encephalitis lethargica and the hysterical symptoms of disseminated sclerosis There is no

mental disorder, mild or severe, in the causation of which bodily disease may not play an important part Moreover it is not only in crude instances of structural or chemical disease that the relationship between bodily and mental illness may be recognised A human being does not exist as a rarefied mind united with a solid body he is an organism all of whose subsidiary functions contribute to this highest function—his mind—which brings him not only consciousness but also an integrated behaviour in relation to his surroundings Disturbances transient or permanent, of these part functions (for example in the sensory apparatus or the circulatory system) will have some effect on his state of mind Changes in the central nervous system are the most obvious instance of this but the endocrine glands the autonomic nervous system and the metabolic processes are often of notable significance in the various maladjustments summed up as mental disorder A human being is constantly responding to and influencing his surroundings but his doing so is conditioned by the various parts of his body and the way they are working It is likewise and equally necessary to weigh psychological influences and effects when deciding the pathogenesis or the treatment of predominantly physical illness The part that emotion may play in the chain of events that cause or aggravate peptic ulcer has been lately demonstrated in a manner to convince the sceptic and there is less dramatic but equally weighty evidence attesting the interplay between psychological and physical happenings which may influence the outcome of many a surgical or other illness Much of the recent enthusiasm for psychosomatic medicine turns on a belated recognition of this It is plain that psychiatric issues must be the concern of all doctors not merely the psychiatrist s preserve and that psychological happenings differ from physiological in their deceptive accessibility to familiar methods of observation in their almost Gordian complexity and in the concepts found most useful for describing and explaining them rather than in any essential quality which would keep them permanently distinct

Before the categories and clinical features of mental illness are described the principles of psychopathology prognosis and treatment call for some very brief consideration since without them psychological medicine written down is a repellent catalogue of details Though the principles set forth may seem trite or too obvious to be worth stating it is unfortunately the case that they are often not applied as fully as they might be to the clinical study and treatment of mental disorders

Psychopathology —INTRINSIC CAUSES —The intrinsic causes of mental disorder are those which depend on heredity and on phases of development *e g* the climacteric Extrinsic causes which come from the environment are either mental experiences or physical damage The distinction between intrinsic and environmental like that between physical and mental is convenient but artificial a long sequence of related happenings both within and without the patient s body goes to the causation of any mental illness It is of course possible in many instances to discover some indispensable link in this chain of causes—an intoxication with alcohol for example a syphilitic infection of the brain an inherited predisposition to periodic insanity a bereavement—which may legitimately be singled out as the chief cause and classified as intrinsic or extrinsic but this is more valuable for formal and didactic purposes than clinically Actual cases usually show a complicated ætiology Thus a man whose parents had both been subject to melancholia became himself profoundly depressed after the death of his wife and attempted suicide by drowning He survived but during the resulting pneumonia he was delirious and threw himself from an upper window crying out that he must go to his wife The causes of the mental disturbance in this case were many and obvious numerous they always are but not always obvious One cause may of course be prepotent

The more detailed the analysis of a patient s endowment and experiences the more entangled physical and psychological internal and external factors seem to be

Heredity and constitution —The hereditary factor is not a general neuropathic

taint there are specific predispositions to one or other anomaly These predispositions are transmitted in accordance with familiar genetic principles summed up in the modern gene theory of inheritance Studies of families and of twins have proved the importance of the hereditary factor in the major non organic psychoses though they have not yet sufficed to reveal with certainty the number and location of genes concerned in the transmission of the hereditary types of morbid reaction

Among the main reasons for this incompleteness in our knowledge is the impossibility of concluding that an inherited trait is not present, merely because it is not manifest in some recognisable form Other inherited factors and most of all the environment will in many cases determine whether an individual predisposition is to become evident or not Thus a man may have an inherited tendency to melancholia which remains latent until a financial reverse or disease of the cerebral arteries provides the conditions necessary for its manifestation It is true that some inherited predispositions e g to Huntington s chorea are almost independent of the environment in this respect but such are exceptional

More than one type of proneness to mental disorder can be inherited by the same person He may for example be prone not only to periodic insanity but also to schizophrenia Mingled proclivities of this kind account for anomalous clinical pictures frequently met with and difficult to classify as either one syndrome or another The ' either or kind of diagnosis is often out of place or misleading in psychiatry because of the commonness with which more than one constitutionally rooted type of illness may be found in the same patient Syndromes are frequently combined, to grasp their clinical meaning one may have to investigate the patient s family not only as to mental disorder, but as to normal characteristics of temperament also

The signs of a transmissible tendency to some mental disorder may not be actual illness but only a special kind of personality There are certain varieties of personality which show some of the essential features that characterise certain types of mental illness, the differences between personality and illness seem then to be of degree rather than of kind Moreover those who manifest one or other type of illness are often found to have had the type of personality that is functionally similar to it So close may the similarity be that it is difficult to decide when the illness has begun because there was no sharp dividing line in time or in form between the more or less normal previous personality and the actual disorder This frequency of association and similarity of form between the normal state and the illness points to the constitutional background of mental illness and shows how hereditary tendencies can express themselves in more or less normal ways in personality before the catastrophe of an obvious illness has directed attention to them Nor is it only in the personality that inherent proclivities may be revealed certain types of bodily structure too occur much more frequently in those with a particular mental constitution or mental illness than in the rest of the population The most striking instance of this is the frequency with which a pyknic bodily habit and a syntonic personality are found among those who have periodic attacks of mania or melancholia (see p 1646) It is not common to find pure examples of mental or physical types in the population and recent work e g that of Sheldon has aimed at making it possible to designate the mixture of components in any individual by a taxonomic formula rather than by ascribing them all to one or other type but whatever method of description be employed the association of osseous and muscular structure with a particular personality structure and perhaps with a predominant form of autonomic response seems frequent enough in healthy as well as mentally ill persons to warrant classing physique physiological behaviour and personality together however tentatively Such constitutional features whether mental or physical indicate that inherited tendencies can body themselves forth in normal physical and psychological structure before morbid exaggerations of them make an appearance The varieties are some-

times called by appropriate names e g schizoid cyclothymic syntonic obsessional hysterical paranoid The relationship is not a simple one There are very many people with these types of personality who never fall mentally ill

A pronounced personality, belonging to one or other of these types does not indicate that the person who exhibits it is likely to have a mental illness but only that if he should have a mental illness it will probably be of the corresponding type As with all inherited anomalies of which the crude manifestation is delayed until adult life there may be for many years none or only mitigated signs of the proclivity these may be indistinguishable from what occurs in normal people The more pronounced the anomaly of personality the more likely that it portends a mental illness, or at any rate a proclivity to the mental illness in specially adverse circumstances

In studying personality, the psychiatrist can have recourse to several techniques besides direct observation and the descriptive method based on the reports of those familiar with the individual studied The most ambitious are projective methods of which the Rorschach ink blot and the thematic apperception test are examples The patient s fantasy is evoked by more or less standardised stimuli and inferences drawn from what he says and does in these circumstances Expert and cautious interpretation is indispensable This applies to the whole of the growing array of psychological methods of assessing personality

In the foregoing personality and constitution have been spoken of as though they were static, innate attributes of the human organism Neither of these epithets however is appropriate not even in respect of bodily constitution Responsiveness and plasticity are essential to human development of every kind there is a constant interplay of personality with the outer world modification of it and by it The main pattern of development is doubtless determined by innate inherited factors—bodily structures grow instincts come into play and the general direction of functional activity is predetermined But general directions and main patterns mean little unless they are given body and content by individual experience Nutrition for example can deflect the body from its ordained pattern or enable its fulfilment all sorts of physical interference can maim it or improve it the same is profoundly if obviously true of the mental side of human growth and maturity Consequently each patient s personality is not to be assessed as conforming to a frozen artificial type but as a complex of dynamic functions changing in outward form sometimes in unstable equilibrium and none the less powerful for being subterranean Here as was said earlier of psychiatry in general there must be two ways of viewing the data in classes and as individual living biographies to be understood rather than schematised Both methods are necessary to any complete psychopathology

Phases of development —A concrete instance of the foregoing is the change that occurs at certain turning points such as puberty pregnancy or the climacteric Endocrine and other physical changes at these epochs may be accompanied by psychological disturbances the severity and form of which bring them under the notice of the psychiatrist They are dramatic episodes in a lifelong process of growth maturity and involution or decay which is marked by plasticity and development of varied functions in the first stage stability and differentiated adaptation in the second emotional lability and suspicion intellectual narrowing rigidity failing grasp and memory in the last The mental disturbances which may occur at different ages are much influenced by these intrinsic factors and tendencies

EXTRINSIC CAUSES —The outer world impinges on human beings from the day of their birth or even their conception in more and more complicated ways as they themselves become more complicated In other words the environment is for the individual as complicated as he can make it and that will depend on how far he has himself developed hitherto Human beings deal selectively not merely passively, with experience At each stage of their growth previous experience helps to determine what they will select from their environment and how they will use this and

integrate it, to serve in its turn as the partial determinant of further growth and integration (the other determinants being innate ones) Experience ' is here being used in the widest sense to denote the response of a human being to the impact of the outer world upon him, whether it be consciously recognised as such or not at the time

It is therefore, impossible to give adequate consideration to any aspect, including the psychological of a human being s way of dealing with the outer world unless one pays regard to his previous experience mental and physical and to the present state of his whole organism mental and physical The cultural milieu in which he has grown up must be taken into account *Too partial a regard for subsidiary functions* whether physiological or psychological may lead one away from the living human being who is an integrated organism not a collection of disparate mental and physical systems similarly *too concentrated a gaze on this latter aspect i e on the socially* organised person to the neglect of part functions may make one see only a dis embodied spirit, as remote from medicine as from daily life

Physical experiences —Some external happenings influence the mental state chiefly by way of the body infection physical trauma intoxication and metabolic and endo crine disturbances due wholly or in part to environmental influences may result in mental disorder In many of these instances the mental change is mediated by way of some cerebral damage and the clinical picture is of the organic neurogenic kind *e g* dementia It would be wrong to attribute the whole of the mental disorder to the cerebral damage, but to it is referable the core of the psychosis Some diseases have an incidence on special functions and parts of the central nervous system which determines characteristic features in the mental picture *e g* the anxious fidgetiness of the patient who has had chorea the stiff mind and obsessional thoughts and move ments of the post encephalitic the hysterical phenomena of the elderly arterio sclerotic patient or the man poisoned with carbon monoxide the aphasia and apraxia of the post apoplectic, the silly moria of the cerebral tumour In the main however it is not possible to correlate mental symptoms with special areas or kinds of cerebral damage—partly because the brain is not the only structure concerned partly because it acts as a whole and also because the presumptive changes in it are too evanescent and delicate to be accessible to our crude methods of examination Even the electro encephalogram which seemed to promise so much has contributed little to the understanding of cerebral happenings in mental disorder other than epilepsy though it is valuable in suggesting the presence or indicating the site of a lesion *e g* in the temporal region

To limit oneself to the brain in studying the somatic correlates or basis of mental phenomena would be an error In the physical accompaniments of emotion the whole body participates through the mediation of the vegetative nervous system and the endocrine glands This is significant because emotional upset is one of the most important phenomena of mental disorder The sequence of psycho physical happenings of which an emotional upset is the climax and the outward sign may be started not only by some mental happening but also by physical experiences—intoxication with a drug or a circulatory disturbance or a metabolic upheaval such as acute hypoglycæmia Whether for example this hypoglycæmia comes from out side as an injection of insulin or arises (as it rarely may) from within the body as a spontaneous deficiency is of little consequence in its bearing on the mental disturbance engendered The chief emphasis lies on the physical apparatus through which so widespread an affection of the whole organism can be evoked just as in other circumstances the emphasis would lie on the psychical apparatus which serves the same end This applies more widely than to emotional disturbances alone Where a symptom is on the face of it *definitely physical or definitely mental* its causation may not be inferred to be exclusively of the same order the chief cause of say an anorexia may be a series of mental experiences or an attack of migraine or

a uræmia or a pituitary disease Study of the anorexia alone cannot serve to discriminate them not even study of the psychological state alone or of the physical state alone may suffice Very often the physical and psychological factors in causation are mingled inextricably—they represent of course different facets of the same series of phenomena

Mental experiences —Mental growth is dependent on daily experience for its material Experience can be subdivided into perceptual emotional and other kinds but such a division is fictitious The means by which daily experience is incorporated with our mental equipment and acquires an influence over our subsequent behaviour in all respects can only be understood if we avoid thinking of emotions instincts perceptions and other abstractions as real entities as distinct and separately operative forces Memory for example is not merely an intellectual function by which we recall a happening into consciousness in more or less verbal terms but a device or function by which past happenings are able to influence subsequent behaviour the ways in which they do so and the form in which the earlier experience is reproduced into consciousness will be greatly influenced by its original emotional as well as more purely perceptual aspects and by other physical and mental experiences—a distressing repetition of the experience for example or a physical happening like concussion or cortical atrophy

There are general needs in mental life—instinctual needs—which bring us into relation with our immediate surroundings lead us to feed ourselves maintain our lives reproduce and aim at other ends which have been variously formulated by philosophers saints and psychologists These biological forces however denominated or classified are not peculiar to human beings but in respect of human beings are so much more accessible to minute enquiry along verbal lines that complex conceptual systems have been built up to describe them Comparative and experimental psychology have partly corrected unreal refinements and highly metaphorical interpretations physiology can also help here Unduly speculative subtleties *e g* some psychoanalytical ones are ill suited to medical needs The influence of previous experience on all subsequent behaviour is as evident in physiological happenings as in the mental field the special language and formulations and hypotheses of psychology are not to be taken as permanently di tinct from those suitable to less highly integrated functions though much must be conceded to the special complexity and character of psychological phenomena Such terms as projection sublimation conversion symbolism identification repression amnesia perseveration displacement of affect cover special instances of the general relationship between inherent tendencies of the organism and their material substrate and the influence of past on present experience and behaviour

In dealing with the multifarious world about him a human being is constantly obliged to select what he will perceive and in what form he will perceive it pure objective perception never occurs To perceive things at all he must give them meaning by relating them to himself and to his previous experience Unless he can do this not necessarily consciously he is at the mercy of his environment as a new born baby is Perception is therefore an active process it has instinctual and emotional as well as cognitive aspects It depends partly upon memory for being able to give meaning to what it perceives such memory need not be conscious Consciousness it is well to bear in mind is only an attribute of psychological happenings not their essence or their criterion mental life goes on with varying degrees of consciousness attaching to it There is no sharp division between conscious and unconscious mental life no region called the Unconscious with its own rules and contents Many of the psychological happenings most significant for psychiatry go on without clear consciousness of them but in appropriate conditions they may be accompanied by much more or by full consciousness Biologically and psychologically regarded consciousness is an attribute like movement or the ability to learn

immensely important for us human beings, but not a 'present or absent factor decisive for our mode of mental conduct

Perception being thus an active process which makes use of past experience it not only selects its material and invests it with meaning but in doing so may distort it and give it a special false meaning Unwelcome emotions may be thus projected on to external objects or happenings, which are then regarded as hostile or contemptuous or in some other way significantly related to one s self This is not remote from the process in visual perception whereby one projects the image on one s retina into the external world and is convinced of its reality there, the further process of clothing it with emotional significance depends on one s inherent tendencies and one s previous experiences Paranoid symptoms ideas of reference, grandiose and *self reproachful delusions exemplify this* Hallucinations and kindred phenomena are a special instance of the interplay between material substrate (*e g* in cocaine poisoning) inherent tendencies (*e g* visual fantasies of children) and past experience (*e g* hallucinations *of homosexual abuse or divine commands*) *Similarly* by fantasy and imagination the outer world can be manipulated or denied according to the heart s desire just as by body images of proposed movement the way is prepared for purposive muscular action In giving meaning to present things personal connections between them and earlier experiences are established, whether normal or morbid this ascription of symbolic' meaning to everyday objects is indispensable to thought, and is most striking in our use of spoken or written language, where sounds and shapes are conventional symbols for the most diverse experiences Some of our words are personal to ourselves and are used in an individual way, in morbidly heightened form this process may issue in schizophrenic neologisms or oddities of expression *Similarly* an obsessional patient may feel towards some word *or object* a superficially incomprehensible mixture of attraction and repulsion which is due to this word or object being the symbol of some earlier experiences that have been of great moment in his life To see how it has come to be such a symbol calls for minute study of his earlier experiences Physical happenings in one s own body may symbolise present emotions or earlier experience of a momentous and emotionally painful kind A gesture of disgust may normally be evoked unconsciously by a banal happening which has somehow become emotionally coloured by past experience A headache or nausea may embody our dissatisfaction with a present situation So hysterical " conversion ' symptoms may reflect and symbolise an inner emotional struggle as may also some obsessional movement schizophrenic stereotypy or *hypochondriacal* fear The body with all its functions is the background of psychic life and resonates to it

What experiences will be important in determining the form of mental symptoms depends much on the emotional disturbance they originally provoke and this in turn on the instinctual drives which they touch on and disturb Instinctual needs may conflict, and the emotion accompanying the conflict prove so disturbing that it cannot be borne in its naked form repression serves the end of making this more or less tolerable through disguising or distributing it So emotion may be shifted from one object to another and paradoxical or unexpected emotions be thus aroused by objects on to which the affect has been *displaced* *Or energy* mainly directed to plain ends *e g* sexual love may be diverted into less obvious channels and when thus sublimated and mingled with features derived from other instinctual sources *its origins* may be hard to recognise Sexual needs so often conflict with others that many of the most powerful motives for the production of mental symptoms come from the struggle

To describe the whole of instinctual life however in terms of sex and aggression as has sometimes been done is only possible if one strains *the meaning of* these words out of all knowledge It is as unwise to make the sexual paramount in psychogenesis as to burke it.

The patient s present symptoms it is clear must be examined in the light of his earlier experience Thus one elucidates in detail the content of his illness and some of the causes of its occurrence In doing so it is not necessary to push back all one s enquiries to a supposedly crucial stage of early childhood The experiences of the first 2 or 3 years of life are like all subsequent experience contributory to mental development and they show certain sequences of phenomena characteristic of such development Moreover their relative simplicity makes it possible to recognise in these early reactions the instinctual drives or (more correctly) the inherited functions which become manifest when the environment supplies the necessary material, though of course it cannot supply the necessary energy and direction these last must come from within On the other hand the functions recognisable in the relatively simple reactions of early childhood are not the same as those which may be seen in later years when the organism is more fully grown any more than an infant s physical structure and functions are identical with those of the more differentiated adult The obvious continuity of the actual happenings in a human being s lifetime does not justify one in trying to analyse and reduce all adult mental phenomena into terms of child psychology nor does clinical practice usually require it

The effect of war and famine upon the incidence of mental illness has obvious importance The psychiatric disorders which occur in war do not differ in kind from those of more normal times but certain forms of disorder especially panic exhaustion psychogenic semi stupor and gross hysteria in men, become commoner and sometimes more severe People are exposed to unaccustomed dangers their privations are both material and emotional they have to surrender some of their independence and individuality and they are thrown together in groups and therefore prone to share in group feelings and group behaviour It is not known whether the losses fears misery and other psychological burdens and cruelties of modern war and its aftermath directly lead to an increase in certifiable mental illness though such exogenous factors as malnutrition and infectious disease which war favours may have this effect It is however neurotic disorders that chiefly excite attention during war as they are then more certain to be ascertained they interfere with military efficiency they can impair morale and a far higher proportion of affected people come under medical scrutiny than is customary during peace

Course and Prognosis —The making of a correct diagnosis may in psychiatry indicate the general drift of an illness—towards recovery chronicity progression or relapse—but is of even less use than in the rest of medicine for showing how far this will apply to a particular patient For this careful study of the individual history and illness are indispensable The prognosis can be inferred from the causes the mode of development and the form of the disorder

Where a known external cause has been at work its point of attack its severity and persistence will affect the issue This applies equally to such organic causes as poisons and cerebral diseases and to mental causes like economic misery or frustrated love The physician must consider how long the environmental cause has been acting what changes it is known to produce—cell degeneration or gloom fibrosis or fantasy—and whether it is likely to persist He must also ask if the patient s previous history has shown that he is specially sensitive to such a trauma This brings in the intrinsic causes How has the patient previously reacted to this sort of interference or to any disturbing circumstances ? Has he fallen more and more into unsatisfactory habits in meeting his daily life and its difficulties ? How has his whole character developed ? Is there good evidence of his being able to cope with partial deviations from mental health ? Has he inherited tendencies to benign or to progressive illness ? Which seem to be the most useful reparative or stabilising features in his personality ? How far are his struggles with the world an outcome of his intrinsic endowment evident in various guises since his childhood how far have they been forced upon him by an adverse milieu ? How old is he ? There is

more chance, if he is young of his being adaptable so that the removal of various stresses may help him and his energies be diverted into less morbid channels, as he grows older he may gain in stability but gradually become more disposed to fear and suspicion bodily preoccupations and fixed attitudes of mind

An abrupt onset is favourable other things being equal A gradual especially an insidious onset may indicate a rooted abnormality that will be hard to shift The longer an illness has gone on, the more will it have become autonomous, *i e* independent of the immediate causes of its occurrence A study of the ups and downs in the course of an illness may show favourable influences that can with profit be deliberately brought to bear on it, as well as harmful ones that must be avoided The more reconciled the patient has become to his illness the less likely his recovery

As to the prognostic conclusions that may be drawn from the form of the illness there is much empirical knowledge at our disposal Thus a predominantly affective attack will very likely clear up but may recur a schizophrenic syndrome is ominous in the long run hypochondria and depersonalisation especially in young people tend to last a long time even years sexual perversities can seldom be got rid of altogether hysterical symptoms can easily be changed but hysterical reactions are persistent, obsessional illnesses are either periodic or very chronic melancholia is often a fatal disease through suicide or refusal to eat delirium tremens commonly ends by crisis or lysis after about 7 days untreated general paralysis of the insane goes downhill towards dementia and death with partial remissions on the way and so forth There is a wealth of such special prognostic knowledge based on clinical observation and statistics

Obviously prognosis must always take account of treatment Will treatment be efficacious ? Will it be practicable ? Will the patient accept it and keep on with it ? It would be absurd to forecast how general paralysis will turn out if one did not know whether one would be giving penicillin or how hysteria would turn out before one had decided whether psychological and social treatment would be possible In every mental illness this is one of the essential points to be weighed in prognosis what will be the conditions beneficial neutral and adverse under which the patient is going to live henceforth and in particular, what specially devised conditions social psychological and physical are practicable and likely to have therapeutic effect ?

Treatment —PROPHYLACTIC —Much can be accomplished by social measures also by individual care though that is less certain A striking instance of social influence in preventing mental disorder may be seen in the drastic reduction in alcoholic psychoses Morphine and cocaine addiction and lead encephalopathy are now rare typhoid delirium is exceptional and typhus unknown It is the organic mental disorders that have been more accessible to these preventive methods so far because they have one indispensable cause that can be controlled The functional disorders are partly due it is true to social causes such as rigid or inappropriate moral and cultural standards bad upbringing and ill judged interference Though the total removal of these is far off there is much room for prevention here A preventable social cause may be well seen in compensation neurosis where the administration of a humane statute involving lawyers insurance companies doctors employers and employees often has the inhumane effect of evoking hysterical symptoms anxiety and a depressive or paranoid invalidism in the injured man

Individual preventive measures cover both the intrinsic and the extrinsic causes Eugenic precautions such as birth control or voluntary sterilisation (if legalised) may under skilled guidance prevent some mentally unstable persons from being born to parents who having had mental illness themselves do not wish to propagate it If physical factors *e g* diabetes be prominent in causation it may be possible to prevent the mental illness or at any rate to scotch it in its early beginnings by dealing with the somatic disorder Thus there are fewer cases of syphilitic psychoses now

that syphilis is less often contracted and earlier treated The psychological reactions to a physical disease or blemish may be favourably modified or averted when fore seen It is for obvious reasons impossible to counteract mental disorder by regularly protecting the patient from physical or psychic trauma in any case a life guarded against risks and painful experiences would be almost certain to issue in mental ill health out of its very emptiness By altering a patient s environment and way of living one may however be able to avert an impending illness only study of the individual patient can show how this end may be achieved Making the patient s environment easier for him may be difficult in some instances because doing so would conflict with his obligations toward other people and even if on balance a change of this sort seems essential the patient may thereafter be troubled by guilt and shame This is particularly evident in unsettled times

The work people do and the conditions under which they do it influence their mental health By ensuring that good vocational advice is available to those about to enter the field of employment and to those whose maladjustment is connected with *their occupation useful preventive work can be done*

How far the treatment of behaviour disorders and neurotic traits in childhood can be trusted to avert outbreaks of definite mental illness in later life is a disputable matter but it is fairly certain that by taking advantage of his plasticity and responsive ness a bent can often be given to the energies of the maladjusted child which will result in his being socially better adapted and better able to deal with his problems The more persistent the beneficial influences one can bring to bear on development at this impressionable age the more valuable the prophylactic effort

Many of the most effective and urgent measures of mental hygiene that may be recommended to the community as a whole are still largely of a negative kind what to avoid rather than what to do This applies particularly in the field of sexual prac tice and belief where needless fears and harmful education are rife as with regard to the masturbation of adolescence—a normal and comparatively harmless phase of *sexual development*

TREATMENT OF THE ACTUAL ILLNESS —This is almost as varied as ætiology There are no specific methods of treatment of sure efficacy nor can treatment safely be limited to one approach whether physical psychological or social There is no valid distinction between palliative and curative therapy the distinction should be between more efficacious and less efficacious The nearest approach to a successful causal therapy is attained with those mental disorders which are closely related in time and form of occurrence to some indispensable cause *e g* a toxic delirium a reactive depression or anxiety an interstitial syphilis of the brain But these are rare condi tions if one considers the whole of mental illness The treatment of general paralysis by artificial fever was not causal its theory was dubious its basis quite empirical yet it was the most important therapeutic advance in psychiatry for a hundred years One cannot despise any measure that promotes the recovery or well being of the patient the giving of drugs the prevention of suicide occupational therapy analysis of motives induced convulsions removal into favourable surroundings hypnosis insulin re education and other means of helping the patient are not to be graded in an arbitrary hierarchy nor should recovery be called spontaneous—as it often is— if it has occurred after treatment which did not include psycho analysis or vigorous physical procedures

Sometimes a patient s condition demands energetic intervention sometimes it demands restrained symptomatic treatment sometimes social adjustment is called for sometimes drugs Whether the accent in treatment shall fall on the physical or the psychological or the social side will often be less important than care that all the available resources are used It should not be taken for granted that a diagnosis connotes a method of treatment *e g* that psycho analysis is the only thorough treat ment for obsessions while for depression convulsant therapy is the proper method

Nor to mention another common error, should it be lightly assumed that a heavily tainted family history or other evidence of a strong constitutional factor indicates that treatment is out of the question a superfluous struggle against fate

Treatment may be considered as social, psychological and physical For some types of illness obviously much more stress will fall on one than on another of these *e g* in hysteria general paralysis of the insane epilepsy

Social and occupational treatment —The first task in social treatment is to decide where the patient is to be looked after Is he fit to be at home should he be in a hospital or in some other environment ? The decision as to the need of a psychiatric hospital rests in the first instance on the danger the patient presents to others or the chance of his committing suicide These two problems of behaviour were at one time almost the only grounds of admission to a mental hospital but such questions of certifiability need no longer preoccupy the psychiatrist since voluntary treatment has broadened the scope of the mental hospital and modern conditions made it suitable for many patients who would ordinarily be regarded as "neurotic" rather than mental, psychotic or "insane" (*e g* early cases of general paralysis masquerading as neurasthenia or obsessionals who fear their own impulses and want to be protected against themselves)

The social decisions in treatment cover much more than merely the mental hospital issue If the patient s immediate environment contains many disturbing influences it will be desirable for him to be away from them temporarily at least so long as this does not entail worse troubles summary decisions are here impossible It may be useless to get a woman who is paranoid about her neighbours to move to another district to escape them unless it is the actual conduct of the neighbours and not the patient s morbid attitude that is provoking her suspicion of them It requires a close knowledge of the facts as well as wisdom and psychiatric experience to give advice on matters that may wholly alter the course of a patient s life—advice, say about separating from his wife giving up his job or emigrating to the Dominions Many instances of this might be offered Neurotic patients are often advised to get married especially if loneliness and sexual needs trouble them as though marriage were a panacea such advice by rule of thumb too often makes their condition worse ruins the life of the person they marry and results in offspring that have to be treated at a child guidance clinic Weary depressed patients are often harmfully urged to go to dances and lively seaside resorts where they must try to look happy Hysterical patients do not benefit by being put among people who are hostile and contemptuous any more than in an atmosphere of mawkish sympathy and compliance

In the social treatment of patients indispensable help can be given by trained psychiatric social workers Their assistance is not restricted to the patient s economic problems No psychiatric hospital or clinic whether for outpatients or inpatients children or adults can do its work effectively unless a psychiatric social worker is a member of its staff to provide expert information and advice on all the social aspects of the patient s illness and to carry out social measures of treatment Similarly a non medical psychologist must be available for help in dealing with educational and vocational problems and the administration of specialised tests

Occupational treatment is important for all kinds of mental disorder Where there is acute overt emotional disturbance rest is at first desirable as also for confusional and delirious states In these conditions opportunity for occupation must be gradually offered to the patient as his disorder subsides steady simple work is preferable to the restless unsatisfying fickle activity in which he would often engage if left to himself The less acute any mental disturbance the more necessary is it that occupation should be urged upon the patient and that it should be disciplined and congenial This applies equally to gross psychoses and minor affections of the neurotic sort Allowance must be made for the patient s bent his symptoms and personality and especially his more or less conscious reasons for working and not

working, hence there will be much diversity in the conditions of his occupation whether it be therapeutically contrived in a hospital offered at a Rehabilitation Unit or sought out as remunerative work in the open market Mental health cannot be permanently retained unless one does some satisfying work often it cannot be re covered unless one does Work is not satisfying in the long run if it is done mainly as a diversion to fill in time

Psychological treatment—There is no form of treatment which has not a psycho logical aspect and result The term psychological treatment or its synonym psycho therapy is however conventionally limited to those forms which depend upon direct and personal relationship between the patient and the physician They have been given separate names and divided into schools and techniques Stress may be laid upon the prestige of the physician (as in hypnosis) the patient s attachment to him in all its complicated phases (transference) the trained understanding and thoroughness with which he clears up the patient s problems (persuasion re-education distributive analysis) or on his qualities of personality—enthusiasm energy warmth candour wisdom In so far as psychological treatment is necessarily based on a personal relationship it cannot be made a routine except in its non essentials whatever rules the psychiatrist follows or whatever the training he has undergone he himself is more important than his method in benefiting the patient To that great extent psychotherapy is not a scientific procedure That is not to say that method and training are of no consequence—far from it—but only that they are devices whereby the influence of one human being upon another s mind and conduct can be turned to the best medical ends and the dangers inherent in such a relationship minimised

The more specialised intricate or esoteric the method the less suitable is it to be used by any but the expert It is not proposed here to detail the many kinds of technique that have been employed The general rules that must be followed in any psychotherapy are

1 To regard the removal of symptoms as a good thing but the maintenance of normal social adaptation as far better It is bad to get rid of one symptom only to see it replaced by another but much worse to get rid of all symptoms only to see the patient at the end of treatment a dependent and introspective hypochondriac of the mind a social invalid

2 To seek for the psychological causes of the patient s illness only to the extent that the patient s well being demands which is often far short of what one s own interest and psychological curiosity would demand

3 To consider carefully whether any shock to the patient any aggravation one produces in his illness even temporarily may be a sign of bad treatment

4 To be satisfied with the patient s recovery and not to aim at his promotion to a state of ideal mental health and self understanding It is better that treatment should be quick and effective than drawn out to meet theoretical standards

5 To understand the development of the patient s illness and to interpret it both to him and to oneself in terms of real experience rather than of hypothetical forces

6 To treat the patient without allowing one s own emotions to be more con cerned in the course and outcome of the treatment than is usual in the treatment of a physical illness

7 To aim at harmonising the patient s mental life by giving his ill managed energies fitter material to work at and release from the burdens laid on them by past experience

It is impossible to describe in general terms what the psychotherapist does other-wise than by *metaphor or analogy he promotes the ventilation and desensitisation* of emotional disturbances he elucidates latent or obvious muddles disentangles conflicting tendencies giving them new incentives and a different direction and so

guides the patient through the maze of his life s experience as recalled in memory that he is then better fitted for dealing with current experience knows himself better and has somewhat purged himself of past harms All analytic' methods review the patient s life as he recalls it under special conditions, *e g* of free association hypnosis biographical scheme, etc They stop at different points some aiming at emotional clearance by abreaction some at a redirection and liberation of the instinctual bases of character, while others remain content with an educational achievement

Whether psychotherapy in the above sense is to be applied will depend on the following factors the patient should be willing to co operate in the treatment, free from such hindering disabilities as say deafness able to give the necessary time, of at any rate average intelligence still capable of modification (as he would not be in old age or with very long standing and indurated habits of faulty reaction or with organic cerebral disease) and finally endowed with a considerable residue of normal mental functions with which one may work The more profound his aberrations as in schizophrenia or the more extreme his emotional disturbance as in agitated melancholia the less is he fit for psychological treatment of this individual and specialised kind Psychological treatment however in the literal and larger sense of the words is essential for every variety or stage of mental illness and every degree of co operativeness or intelligence It is a wide notion including all that may ease or reassure the patient bring him to a better relationship to those around him and with himself and protect him from being distressed by the ignorance lack of tact or thoughtlessness of others It is as much negative as positive One must avoid arguing with the patient, telling him lies for his own good or to avoid unpleasant scenes cajoling him making promises that will not be kept threatening or punishing him jesting at his expense losing one s patience with him assuming he is indifferent to what goes on because he looks indifferent provoking him by petty supervision or frequent rebukes, one should not assume that he is quite irresponsible or quite responsible nor talk theory to him nor get on a false footing through ready assent to his delusions and his point of view The physician and the rest of those who are in contact with the patient must do certain positive things make due allowance for his disorder influencing his conduct use their understanding of the psychological happenings without saying so take advantage of every opportunity created by other methods of treatment When occupation narcosis hydrotherapy a course of insulin, massage a physical illness or other happenings bring him more closely into contact with nurses and physicians there are chances of unobtrusive psychological treatment in the wide sense

Of late much effort has been put into treating patients not as individuals but as members of a group Though less economical of time and labour than had been hoped this has the advantage of utilising for therapeutic purposes the influence that patients have on one another Many devices have been employed from social club meetings to psycho drama —plays that originate with the patients and touch on their conflicts and are followed by a group discussion The procedures are still experimental and have not made individual treatment superfluous

Physical treatment — Mechanical restraint and violence are now foreign to the treatment of insanity the patient may be unrestrained and violent but his treatment may not It is still necessary however to restrain a patient who is bent on harming himself or others and physical force may be the only way of doing so or of giving a patient by tube enough food to keep him alive when he abjures the natural way of eating But force must always be a last resort and chemical substitutes for it seem only a little less of an evil Drugs have their place in the treatment of all kinds of mental disorder but their use easily turns to abuse Whether one is giving morphine and hyoscine in an emergency to an acutely excited catatonic or prescribing aspirin for a mild hysteric the chief danger which must be borne in mind is not over

dosage habituation or suicidal misuse but the habit of stupefying or satisfying a patient with drugs when other means might be taken better suited to his condition Sedative drugs should not be a short cut neither should they be eschewed They should be given when other measures will not serve as for some obstinate form of insomnia anxiety agitation and restlessness or when their use obviates greater troubles *e g* the pulling of bandages from an operation wound The symptoms of intoxication must be watched for with more than usual vigilance when bromide is being given because if unrecognised as such they may lead to certification—for an avoidable drug made psychosis Continuous narcosis for several days with the patient sleeping through 18 or more of the 24 hours is sometimes efficacious in abbreviating an acute attack of mental illness or giving complete rest to an exhausted very anxious person it is not without risk except in skilled hands

There are other drugs to which the above cautions scarcely apply *e g* endocrine preparations remedies specific and otherwise for the physical basis of organic psychoses (*e g* arsenical treatment for syphilis of the central nervous system) and aperients Insulin for promoting hunger calcium for those with hysterical hyper ventilation fits amphetamine (Benzedrine) and acetylcholine for anxiety and a number of substances—from nitrous oxide to amylobarbitone (Amytal)—that relieve catatonic stupor or facilitate psychological enquiry and treatment have all been found useful on occasion Recently hypothermia induced by chlorpromazine (Largactil) has been employed but its value is highly doubtful The same may be said of malononitrile

Three methods of physical treatment have been introduced and widely employed since 1935 namely (1) insulin in large doses to produce hypoglycæmic coma re peatedly (2) convulsant drugs and latterly, electrical stimulation of the brain to bring about fits and (3) surgical incision of both frontal lobes—leucotomy—to sever the connection of the anterior portions with the thalamus Although the former procedures and their many modifications are often referred to by the single ill chosen term shock therapy they have little more in common than that they are crude empirical methods of altering mental disorder for the better their *modus operandi* being still a matter of conjecture Since the insulin method demands skill and experi ence if considerable risk to life is to be avoided it has not been so much used as convulsant treatment Its field of application is schizophrenia especially the early acute forms with good prognosis Convulsant treatment is now given almost always by the electrical method Though first devised for schizophrenia it has limited success there except in the acute stuporose forms and those associated with an affective syndrome Its efficacy in involutional and some other affective disorders is however striking It terminates obstinate melancholias and abbreviates attacks of depression which would otherwise take many months to clear up

Frontal leucotomy has a more insecure place as yet than the other two methods It has been or should be restricted to patients who seem proof against other forms of treatment *e g* those with chronic agitated depression long standing schizophrenia accompanied by violent outbursts or intractable obsessional disorder The pro portion of deaths in a fairly large collection of cases has been between 3 and 4 per cent of recoveries (obviously dependent on the patients selected for operation) about 25 per cent another 40 per cent are said to be clinically much improved about 65 per cent of those operated on do not improve sufficiently to leave a psychiatric hospital The procedure does not reduce formal intelligence but blunts spontaneity and control and may impair judgement and foresight it may lead to epilepsy (in from 4 to 8 per cent of cases) or urinary incontinence Some of the successes attained by the operation in apparently hopeless cases indicate that its uncertainty and crudity do not put it out of court modifications in the site and extent of the cut are still being made with promising results

The three forms of intervention described stand or fall not by appeals to general principles or evidence that they are rational and safe but by proof of their value in

alleviating specific types of mental illness They evoked a somewhat uncritical enthusiasm and hopefulness in some who had previously been given to ill informed nihilism about the prospects of any treatment consequently the mistaken notion has gained ground that before the advent of these methods patients who got well must have done so " spontaneously , and that unless a mentally ill person has had ' shock therapy ' or ' psychotherapy he cannot be said to have had any treatment at all

Exercise or massage and hydrotherapy are beneficial as much for their psychological as for their physiological results the latter, however are not negligible as may be seen in the effect on an excited or an anxious patient of a continuous bath at body temperature The chief importance of diet lies in the frequent refusal of food by patients depressive hysterical, stuporose paranoid, hypochondriacal or overactive Feeding by the nasal or œsophageal tube is a necessity in many such instances after every other method has failed Rarely a special diet is called for as in the symptomatic psychoses of diabetes pernicious anæmia or pellagra and also for some temporary disabilities of the alimentary tract As a rule however such dietetic regime and indeed all physical treatment of localised psychogenic disturbances of function in a bodily system, is an expedient rather than a settled and adequate mode of treatment Many patients with a visceral neurosis (e g effort syndrome) a hypochondriacal preoccupation a hysterical anomaly or a somatic delusion are greatly harmed by the prolonged physical investigation and treatment they receive it confirms the symptom localises it all the more and brings fresh ones in its train Sometimes one has no choice a progressive hysterical contracture a dermatitis artefacta a sore infected by constant picking a tooth loosened by obsessional knocking at it demand treatment

The caveat against lightly resorting to physical treatment of psychogenic anomalies is especially applicable to operative surgery, e g ' cleaning up the septic foci '

CLASSIFICATION

The ideal classification would be on a uniform basis according to the nature of disordered physical and psychological function, or according to innate and external causes Since we do not know enough to do this a mixed ætiological functional and clinical grouping is used It is obviously provisional The chief division is between those mental changes accompanying distinctive somatic disorder and those for which no such physical relationship has been demonstrated The former are called symptomatic, or organic the latter constitutional or functional It is needless to illustrate the point that everything found in the latter may be seen also in the former The reverse of this is not true because there are some symptoms—due to the loss or damage of essential tissues especially in the central nervous system—which can only occur when the material substrate is grossly damaged

Although the functional group is made up of those conditions for which no distinctive somatic disorder can be found responsible it by no means follows that their causes or basis are therefore purely psychological Theoretically such a belief is untenable, since physiological and psychological are only different facets of the same phenomena, and as a matter of observation certain physical disturbances so regularly accompany these disorders and a physical configuration may be so linked with them that there is small doubt that eventually the somatic disturbance of function in them will be well enough worked out for the terms organic and functional to lapse and only the crudity or transience of the physiological changes remain as a point of difference

The first or toxic organic group is large the chief syndromes in it being neurasthenia confusion and delirium and dementia Such phenomena as apraxia aphasia agnosia amnesia and hallucinosis are fairly frequent in this group

The second group comprising three fourths of the recognisable mental illnesses includes the insanities or psychoses and those anomalies outwardly less alien to the normal mind commonly called neuroses The distinction between neuroses and psychoses is at times convenient but without substance To argue whether a dubious case is neurotic or psychotic is like arguing whether a man of medium size is thin or fat he is both and neither A genuine decision as to ætiology prognosis or treatment turns not on whether a case is regarded as neurotic or psychotic, but on more solid findings Since such words die hard the best use of them is to term a patient with mental disorder neurotic if he has fair insight into his illness is co-operative and unlikely to need care in an institution and to term him ' psychotic if the contrary is the case

The toxic-organic group is divided into diseases located in the nervous system and those affecting it indirectly as uræmia or lead poisoning may Some are toxic *e g* delirium tremens some degenerative (senile psychoses) some inflammatory *e g* encephalitis lethargica some plainly hereditary *e g* Huntington s chorea or primary mental defect and some privative *e g* pellagra or myxœdema

The functional conditions are arranged according to whether emotional disturbance is evident and predominant (affective disorder) or whether there is profound derangement of thought, feeling and contact with the real world (schizophrenia) morbid false beliefs have become fixed without intellectual or emotional deterioration (paranoia) repetitive and seemingly irrelevant phenomena hamper mental activity (obsessional) signs of physical or mental ill health especially dissociation readily appear when an unpleasant situation may thereby be escaped from (hysteria)

As will be seen in the special sections, the personality of the patient may also be a criterion of these groupings with the proviso mentioned earlier that illness does not only occur in those with the appropriate psychopathic anomaly of personality nor does the latter by any means regularly issue in definite symptoms Unless however psychiatry takes account of the psychopathic personality even when not accompanied by symptoms of illness it cannot study delinquency disorders of behaviour in children sexual perversions and other anomalies which touch very closely on psychiatric problems in the stricter sense

The following is the classification used here it is much less detailed than that of the International Statistical Classification to which however, it can readily be assimilated

Organic Disorders

- Degenerative and Hereditary Brain Disease
  - (Senile dementia cerebral arterial disease and hypertension Huntington s chorea)
- Syphilis of Central Nervous System
- Other Cerebral Diseases
  - (Lethargic encephalitis Sydenham s chorea disseminated sclerosis cerebral tumour cerebral trauma epilepsy etc)
- Intoxications
  - (Alcohol morphine cocaine bromide etc)
- Infections and Exhaustive Disorders
  - (Infectious toxæmias hæmorrhage etc)
- Metabolic, Endocrine and Visceral Disorders
  - (Diabetes pernicious anæmia pellagra exophthalmic goitre myxœdema tetany pituitary diseases sexual epochs cardiac disease uræmia etc)

Affective Disorder

Excitement
Depression
Anxiety

Schizophrenia
Paranoia
Hysteria
Obsessional Disorder
Psychopathic Personality
Mental Deficiency

Mental deficiency instead of being treated as quite separate from the other classes might logically be distributed among them Most of the feebleminded are probably ' sub cultural that is they represent the lower end of a curve of normal distribution of intelligence throughout the whole population intelligence being here comparable with height But just as there are dwarfs whose brevity is not a physiological attribute but the consequence of disease so there are many defectives (almost all idiots fall into this class) whose low intelligence is the result of demonstrable interference with *cerebral development sometimes from hereditary* and sometimes from environmental causes Members of the sub cultural group which is by far the more numerous have it in common with people of psychopathic personality that they are not con spicuously different from the average population they are not ill and their troubles are partly due to and manifest in their social relationships not least during childhood The pathological groups could be systematically classified according to the disease responsible for their maldevelopment they differ from the other organic forms of mental disorder only in the age at which the damage has been done Congenital syphilis cretinism cerebral trauma encephalitis epiloia cerebro macular degenera tion microcephaly gargoylism *hydrocephalus*, epilepsy Huntington s chorea con genital diplegia a long list can be made of the diseases which will interfere with normal cerebral and intellectual growth, if they can begin to act early enough Custom and convenience however are arguments in favour of keeping all mental deficiency in a class by itself

The above are great clinical groupings types of morbid reaction which are as near to a valid and useful classification as we can get at present There are subordinate symptom complexes or syndromes which are likewise innate and preformed and likewise evoked by circumstances but which are not limited to any one of the major groupings—they are the weft that runs across the psychiatric pattern The most important of these are depersonalisation hypochondria twilight states stupor and other disorders of motility and spasmodic attacks and seizures of different kinds Between symptoms (classified on a psychopathological basis) and the main groupings which best serve clinical purposes these symptom complexes have an intermediate place comparable say to that of mononuclear leucocytosis or coma in general medicine

ORGANIC DISORDERS

GENERAL DESCRIPTION OF TYPES

The varieties of form and course in organic psychosis are essentially few and simple in contrast to the causes which are numerous In other words there is no support for the expectation that to each physical disease there corresponds a characteristic mental disorder It is not possible in an organic psychosis by study of the

mental picture alone to infer its physical cause for that the methods of somatic medicine are needed Many different poisons and lesions may produce the same effect on the mental state Differences depend on the degree and duration of the physical damage and its site which may determine neurological and other symptoms of a typical kind *e g* in G P I or encephalitis lethargica

They are the least constitutional of all mental affections yet even in them con stitutional factors are far from negligible It is due to such factors that one man will show a psychosis with physical illness that in another would lead to no such mental upset and that one patient responds with a manic extravagance to the cerebral disease that makes another patient depressed Moreover hereditary factors can be of great importance in these organic affections as may be seen in amaurotic idiocy or Huntington s chorea

The few syndromes commonly met with here though they are not restricted to organic disease must be described before seeing how particular diseases colour them and determine their course and treatment In organic syndromes a diminution in mental capacity is the central finding To some extent these syndromes may occur also in patients in whom no structural damage can be found as might be expected seeing that the available patterns of structure and function are in all cases much the same

(1) NEURASTHENIA —This term has been over used and ill used like most of the more palatable diagnoses (cf anxiety neurosis) but it need not therefore be discarded now It denotes a form of irritable hypersensitive weakness and depression that is not uncommon after infections exhausting experiences (*e g* hunger lactation in somnia worry hæmorrhage) cranial injuries and chronic poisoning (*e g* with alcohol or coffee) It is true that a clinical picture indistinguishable from it frequently arises where physical causes are unlikely and emotional causes are obvious this clinical finding has the same significance as the fact that the anxiety of exophthalmic goitre is like psychogenic anxiety Just as the anxiety of exophthalmic goitre or constant fear can pass into delirium so can physiogenic neurasthenia be aggravated until it becomes plain *dementia*

The symptoms are partly somatic—active deep reflexes increased sensory irrita bility feelings of pressure on the head and pains in the muscles and elsewhere giddi ness vasomotor lability delayed peristalsis and feelings of fullness in the abdomen diminished libido slight clumsiness and tremor of the muscles of the face tongue and hands On the more psychological side there are feelings of languor and in capacity to concentrate on any mental work doubts as to the accuracy of memory loss of interest slight depersonalisation irritability and tenseness lessened control of emotion and perhaps slight paranoid obsessional or hypochondriac trends This general condition is when physiogenic less influenced by a change in mood than would be the case with psychogenic neurasthenia and the patient is better able to control his motor unrest than his features which are expressive of his agitation The chief reliance however must be put on the history and physical findings for telling whether the neurasthenia is physiogenic or not psychological causes which seem adequate to explain the illness may be deceptive

The course of neurasthenia is towards recovery unless the noxa continues to act where the noxa persists extreme chronicity can result Sometimes an original physical noxa ceases to act but meanwhile other emotional ones have entered the field *e g* unemployment domestic fears and frustrations and so the illness drags on Treat- ment depends on assessment of the causes and the possibility of removing them

(2) DELIRIUM —Delirium most familiar in fevers can also be produced by drugs and other causes of acute cerebral disturbance severe affective disturbance also may be accompanied by delirium Its characteristics are general malaise restlessness irritability and sensitiveness to external stimuli headache anxiety and troubled sleep or insomnia Mild forms of this are met with in so transient an affection as cold in the head Severe forms are marked by illusions and hallucinations of all the special

senses, especially vision Anxiety often becomes extreme and the patient is terrified of his fantastic visions Thought becomes as chaotic and fleeting as in dreams activity is incessant and past *experiences of daily life are revived* as *in the* occupational delirium of alcoholics Attention is weakened and orientation in time and space much impaired There are striking variations in the severity *of the condition in the same patient* it becomes worse in the evening or when the patient has hardly any external stimuli to keep him in touch (cf delirium at night and after a cataract operation) The extent to which consciousness is clouded usually corresponds to the amount of perceptual and affective disturbance Auditory hallucinations occur with clearer consciousness visual ones very profusely with a clouded mind The auditory hallucinations are commonly of an elementary, undifferentiated kind—not *voices* Vestibular hallucinations may occur *e g* of floating in the air Distressing and incoherent ideas pursue each other—ideas of being torn to pieces burnt poisoned buried alive and so *on also ideas of grandeur*

Closely akin to delirium and indeed shading into it is the state of clouded consciousness (or confusion) in which thought is *very incoherent* but the patient is *more* eager to get in touch with his environment than in typical delirium If consciousness is not too grossly clouded the patient is perplexed and troubled by the disordered perceptions through which alone he can learn what is going on about him The picture may be indistinguishable from that seen in some forms of manic excitement and in some catatonic states Differentiation rests not on the immediate psychiatric symptoms but on the history and discoverable causes of the illness The same is true of *acute hallucinosis* in which orientation and grasp are very little impaired but auditory hallucinations—especially threatening sounds and voices—abound and there is a tendency to the *formation of delusions on the basis of these and other perceptual* disturbances The name *twilight state* is applied to another syndrome in which consciousness is changed chiefly because of some powerful affective influence anger or fear may so overwhelm psychic life that the patient cannot grasp his surroundings his thinking is interrupted and slow (except where it falls in tune with the affective disturbance) and his motor behaviour is in keeping with his mood It is as often of psychogenic as of organic origin—one can hardly, for example by direct observation tell an epileptic twilight state from an hysterical one Like delirium and the other conditions just mentioned it is prone to subside and to be followed by amnesia for what happened during *it where there is some recollection* it may be *associated with* a conviction that the hallucinations and other morbid phenomena were real external *happenings*

(3) DEMENTIA —Of all gross encephalopathic syndromes this is the gravest and most typical It corresponds to a diffuse cerebral disease and is made up of intellectual impairment and lessened control of emotion Its form depends so much on the stage of the patient s development at which it occurs that it is customary to consider as dementia only those *cases in which the cerebral damage* has occurred in later childhood adolescence or adult life and to regard earlier cases *e g* cretins as showing mental deficiency or arrest of development *The distinction is rather artificial* at whatever age it be made For convenience only the adult form will be described here *The order in which functions are impaired* corresponds to Hughlings Jackson s principle of dissolution thus recently acquired memories are soonest lost. There is intellectual weakness—the patient cannot reason grasp and remember as he could his attention is less concentrated and sharp his ideas are fewer he cannot take in anything complicated or be sure about time and place he loses himself His emotions are likewise affected—he weeps over trifles in spite of efforts *to control himself* his feelings are shallow and transient, he may be foolishly euphoric, or may burst into anger whenever he *cannot get his own* way There are wide variations in the severity of the condition and its symptoms may be much influenced by the local incidence of the pathological changes in the brain The extent to which various cerebral func-

tions are impaired may differ widely in the same patient a man who seems hopelessly demented may be able to play a good game of chess, while another in whom it is hard to demonstrate any intellectual impairment may micturate into his shoes or do something equally stupid and inappropriate, unexpected sexual misdemenaours are not uncommon in demented persons who do not as yet show gross intellectual damage

Psychological tests have been increasingly used in dementia Although they are untrustworthy for diagnostic purposes they can be of value in measuring the degree and progress of the impairment The most convenient method is that devised by Babcock in which the discrepancy between vocabulary score which is often well preserved in dementia and performance on non verbal tasks is assessed More elaborate differentiation by means of a wide variety of tests is still in the experimental stage

Closely connected with dementia are the *amnesic* syndromes known by the name of Korsakoff Here the memory disturbance is in the forefront The incapacity to receive store and reproduce experience is remedied as it were by lying *i e* the patient confabulates to fill up the gaps in his memory These patients are often ready to adopt suggestions so that one can lead them to tell absurd tales about their recent movements *e g* that they were yesterday in Greenland to see some polar bears They do not show an intellectual damage or incapacity to deal with ideas that is at all comparable in degree to their memory disorder but they are always out in their appreciation of time relationships especially where the present is concerned At first blush they often seem to be behaving like mentally healthy people but one presently discovers that their memory is much impaired their orientation as to space time and personal identity correspondingly poor and their interest and general mood duller than is normal The disorder of memory is never, as in dementia a general weakness reaching back even to childhood

The Korsakoff syndrome is most often seen in alcoholics in whom it was first described associated with polyneuritis but it also occurs in a great variety of organic disorders *e g* intoxication with lead carbon monoxide and other poisons uræmia vitamin B_1 deficiency cranial trauma cerebral syphilis and arteriosclerosis—apoplexy may precede it and the amnesic syndrome be thus complicated by aphasia That it should sometimes follow on delirium is not surprising since in delirium the same memory disturbance is present but covered up by the concomitant excitement disturbance of consciousness and hallucinations Whether a Korsakoff syndrome will clear up depends on the cerebral damage which produces it the alcoholic form occasionally does so eventually in uncomplicated and treated cases

Mental deficiency in some of its forms is a special instance of cerebral impairment as is dementia It is considered for the sake of convenience and tradition in a separate section (see p 1682)

DEGENERATIVE AND HEREDITARY BRAIN DISEASE

There is a group of disorders occurring in late middle life and old age which are clinically and even pathologically near to one another At the one end of the scale is senile dementia at the other climacteric anxiety and depression It includes Pick s presenile dementia Alzheimer s disease cerebral arterial disease and arterial hypertension

The mental disorders of age have displaced schizophrenia and manic depressive psychosis from their position as the mental disorders of highest incidence When first admission rates per 100 000 of the corresponding population have been computed either for senile psychoses or for psychoses with cerebral arteriosclerosis a higher figure has been obtained than for the incidence of all other psychoses

combined, the chances of becoming thus mentally ill therefore are higher in the elderly population than are the chances of developing all other mental illness in any age-group of the population If present trends continue the number of persons over 45 years of age admitted to English mental hospitals in their first attack of insanity will by 1971 approximate to the total number of first admissions of people of all ages in 1937 more than a third of these admissions will be of people over the age of 65 It is not extravagant to say that nowadays insanity is mainly a disease of old age

1 SENILE AND PRESENILE DEMENTIA

Ætiology —Constitutional factors are obviously the most important A tendency to become dotards may be evident in successive generations of a family heredity is held responsible for the wide differences in mental health among elderly people The symptoms of senile psychosis may not be revealed until the patient is exposed to some sudden stress—the death of his wife the need to move house the loss of his occupation, some new set of circumstances Social factors are of great importance Senile psychoses are more common in people with lifelong nervous symptoms or psychopathic personality

Pathology —PHYSICAL —The tissues show the general signs of age, *i e* a diffuse atrophy, which makes the convolutions narrower and the weight of the brain less The nerve cells and fibres are fewer while the mesodermal and neuroglial tissues are increased fatty pigment accumulates There are also, however in senile dementia striking histological features in the grey matter especially of the cortex namely thickening of the neurofibrils which are characteristically twisted and aggregated, and there are remarkable plaques seldom seen except in this condition The main change is probably in the brain colloids so that condensation and coagulation take place the plaques and thickened neurofibrils are secondary to this There is no close correspondence between the kind or extent of the tissue changes and the mental state Plaques and neurofibrils can occur also in the brains of mentally healthy old people

PSYCHOLOGICAL —The previous tendencies of the patients may greatly colour the symptoms Obscure somatic preoccupations and disturbances in time appreciation lead often to fantastic delusions about eternity and what is happening in their body

Symptoms —Memory is poor for recent events the extent of the damage may increase until only the recollections of childhood and early adult life remain People and places are falsely identified with those once familiar and transient pseudo memories are invented Events with a strong affective tone especially if unpleasant, are remembered better The memory of the remote past is not entirely spared even matters of personal identity may at last be forgotten Grasp and judgement the capacity to follow a train of thought and to eliminate the irrelevant are faulty Obstinacy and perseveration go with a rigid adherence to old habits Prolix and garrulous the patient does not recognise how little interest there is for others in his repetitive and ill arranged talk He may partly cover its emptiness with long and sounding sentences on the other hand some patients become monosyllabic because of their failure to find words to express themselves and others again will use a word loosely associated with the one they are vainly seeking or will quite seriously give a punning meaning to a word and even act accordingly (*e g* whistling because You said I could whistle for my money)

There is a narrow range of interests in which food possessions and bodily well being are prominent Grotesque hypochondriacal delusions are common Patients hoard rubbish and are angry if interfered with in this On the whole, however their affective responses are greatly reduced they meet calamities with composure partly due to their failure to grasp what has happened Now and then they show depression and resentment at a slight, and may bear a grudge long after Their activities are

sometimes considerable on the lines of determined rummaging and collecting in others a dull inactivity is all They become dirty and unable to look after themselves This applies as much to those who are excited and active as to the inert The former may fight against being fed and washed, and it is not possible to get them to understand what is being done Delirium and confusional states are prone to occur at night accompanied by fear and bewilderment Sleep is bad and often the patients busy themselves about the place all night long

Legal difficulties arise through the heightened readiness to accept some suggestions (as in the matter of making a will or giving away property) the poorer judgement and the lessened capacity to control sexual desire which is sometimes seen in the early stages Hoarding may lead to petty thieving Occasionally the patient sets fire to the house during his nocturnal prowlings

The symptoms need not be obvious Often the illness has so slowly developed that no one can say when it first passed beyond what is normal in old age An apparent change of character—a kindly man becoming selfish a respectable churchwarden assaulting little girls sexually—may usher it in this is not so much a change in character as a release of primitive trends hitherto controlled The psychosis may take various forms—depressive manic and paranoid In the *depressive* variety there is seldom retardation the affect is rather empty the patient is irritable and hysterical symptoms may be commingled with hypochondriacal ones Ideas of poverty wickedness and disease are often grotesque in their exaggeration—the patient s urine drowns the whole world his body is an undying shell of corruption he is as tiny as a baby—and are monotonously reiterated The *manic* variety is rarer pointless activity and a diarrhœa of words with silly boasting may be accompanied by a disturbance of memory giving a total picture of the Korsakoff type it is sometimes called presbyophrenia Many of these patients have always been of hypomanic temperament their illness may be only slightly progressive and not so severe as to call for hospital care The *paranoid* variety is especially likely to occur in people who have always been of a suspicious turn of mind They hide things because they feel surrounded by thieves and then forget where they have hidden them their failing senses especially of hearing feed their distrust and they project their awareness of sexual impotence or waning intellect Hallucinations and delusions are mingled—gases are pumped into their room their food is poisoned people throw bombs at the house by night greedy heirs are doing them out of their possessions Some of these patients barricade themselves against their enemies or call in the police Whereas the depressive and manic forms are commoner in people with corresponding heredity this paranoid form is genetically often connected with schizophrenia though the distinction between the three varieties is not a sharp or important one The name involutional paranoia has been given to the chronic delusional condition of this type that may develop in single women between the ages of 40 and 52

Bodily symptoms are those of old age especially in the central nervous system where it leads to a slow careful gait with short steps and legs wide apart apraxia and poor co ordination tremulous rather whining utterance small sluggish pupils and occasionally epileptic seizures The disorder of movement is conspicuous in the handwriting—pointed small or erratic in size and sometimes jerky and tremulous

The conditions known by the names of Pick and Alzheimer are to be regarded as atypical senile or presenile psychoses

Pick s dementia consists pathologically of a circumscribed cerebral atrophy mostly in the frontal or the temporal lobe or in both the motor area however is seldom affected nor are Wernicke s zone and the transverse temporal convolutions other areas of the brain especially the parietal may be involved Histologically the ganglion cells are swollen and contain argentophil globules There is a hereditary determinant It is almost twice as frequent in women as in men—the opposite of what has been found to hold for cerebral arteriosclerosis The onset which is

gradual can be at any age from 40 onwards but is usually between 50 and 60 Symptoms depend on the localisation of the atrophy Memory and affect are not impaired till late, they are preserved at a stage in which the patient behaves stupidly—stealing lying or otherwise making a fool of himself Spontaneous attention is poor at first moody the patient becomes dull and unresponsive judgement deteriorates and initiative fails Stereotypies echolalia and repetition of empty phrases monotonous talking and laughing or singing and outbursts of bellowing or whining appear in the later stages There may be aphasia Diagnosis is difficult during life it may be assisted by an encephalogram showing the shrinkage of cerebral tissue from atrophy or by biopsy The condition may last from 2 to 12 years

In *Alzheimer s disease* the senile plaques and neurofibril changes are very numerous The onset may be between 40 and 60 Women predominate Indefinite premonitory symptoms (headache irritability forgetfulness) are quickly followed by progressive dementia aphasia and apraxia are prominent though less coarse and sudden than in cerebral arteriosclerosis In the earlier stages the patients are in fair contact with their environment and look as though they grasp much more than they actually can Their deficiencies are shown up in writing and talking They may be restless and depressed As the disease advances they are less open to affective influences they sink into themselves and say little Stereotyped words or syllables and movements take the place of embarrassed remarks and gestures In the aphasia there is a rather characteristic stringing together of syllables like each other in sound but meaningless Muscular rigidity may lead to contractures The progress of this disease to severe dementia is faster than in typical senile deterioration and the onset is rather earlier

Prognosis —This depends on the previous rate of development of the condition the general physical health of the patient and any special pathological basis *e g* Pick s atrophy that may be recognised Delirious and confusional phases may give a deceptively bad impression for sometimes after they clear up the patient can resume his old routine tolerably well

Treatment —Since the breakdown of old people is often brought about by their inability to cope with the demands and stresses of a society that is organised for younger people social measures can do much to delay the time when senile mental changes will make special care necessary The more satisfying their mode of life the less will maladjustment and gross failure be the effect of their senility Although when senile dementia is clearly evident treatment will partly consist in providing as easy familiar and considerate an environment as possible it would be harmful to leave senile patients idle because they seem listless or to let them be lonely because they are fretful Whether institutional treatment is necessary depends not only on the mental impairment but also on the patient s social level and the willingness of his relatives to look after him well enough Patients often fit surprisingly well into hospital life and routine when this makes due allowance for their infirmities and provision for their social and psychological as well as their physical needs Drugs are best avoided and caution is necessary in letting the patient have the aperients he demands to relieve his—mainly delusional—constipation

2 CEREBRAL ARTERIAL DISEASE AND HYPERTENSION

The characteristic features here are the focal symptoms All else is indistinguishable clinically from senile and other cerebral conditions of course pathologically many senile brains show arterial degeneration too The early or mild symptoms of cerebral arteriosclerosis are the same as those of essential hypertension and very like those of many benign melancholias of late middle age

Pathology —Atheroma of the cerebral arteries is accompanied by nutritional changes—softening—in the brain tissue falling into three stages viz necrosis degeneration (with masses of granular phagocytes containing fats and hæmosiderin)

and sclerosis (in which cavities and scars of glial astrocyte and mesodermal tissue take the place of the necrotic cells) (see also p 1443) The cortex on the convexity of the brain may show microscopic areas of perivascular gliosis but no softening It is not yet possible to correlate the mental and the cerebral changes in these psychoses except for the focal lesions

Symptoms —Since "essential hypertension often precedes definite vascular disease and itself produces mental symptoms a description of these symptoms serves also to describe the earlier stage of cerebral arterial degeneration Along with head ache giddiness tinnitus faintness and insomnia there may be disturbance of speech and writing—the former becoming slow and at times indistinct—and transient pareses and apraxia Certain traits of personality may be intensified the patient becomes irritable egotistic moody and easily tired his conversation lumbers along where once it moved easily he is depressed or paranoid but there may be wide variation in the intensity of these changes which are by no means always found Brief phases of disturbed consciousness lasting up to 3 weeks may suddenly occur either in a form very like the absences of the epileptic or as twilight states with hallucinations ecstasy incoherence disturbed motility and agitation

After this stage of neurasthenia and episodic disturbances the patient with cerebral vascular disease may begin to have trouble in finding words he perseverates a little and is *at a loss when anything unusual is required of him His depression and hypo* chondriacal worries increase he is distressed by his own slowness and failures and may attempt to kill himself Emotional control falls off so that he weeps and storms when he would rather be calm Nihilistic ideas may abound—his bowels have not been opened for 6 months his trunk is a hollow cavity Nocturnal delirium is fre quent Aphasia and apraxia are commonest after a focal complication

The most important feature is the way the patient continues to look normal and sensible when already mildly demented Sometimes transfer to the strange surround ings of hospital is too much for the hitherto well preserved outward normality and the patient goes to pieces as he also may if he has to give up his usual work or move house

Diagnosis —Because a patient has generalised arterial disease it does not follow that any psychiatric symptoms he may show are due to the cerebral vessels being thus affected Unless there are definite focal symptoms or evidence of dementia it is unsafe to hold the cerebral arteries responsible and to give a prognosis based on this There is no known means of distinguishing many benign neurasthenic depressions and involutional hypochondrias from those due to disease of the cerebral vessels If there has not been any history of such tendencies until an attack at the age of 60 odd the probability that it is an organic vascular disease is much higher The dis- tinction is all the more difficult because so many unstable persons develop arterial disease in later life especially those prone to anxiety and other affective disorders Neurological findings (see p 1443) may be decisive in a doubtful case The condition of the retinal arteries is not a reliable guide

Course and Prognosis —In definite cases of cerebral arterial disease with mental disorder the prognosis is necessarily bad though the mental symptoms may only progress slowly and the patient live another 10 or 20 years Much will depend on such sudden accidents as thrombosis or hæmorrhage An episodic confusional state perhaps even one produced by drugs may suggest a needlessly gloomy prognosis In cases of essential hypertension the course of the mental illness is dependent on the general disturbance and is often quite favourable Symptoms that are appar ently hysterical occurring for the first time in middle life are of bad omen

Treatment —Besides the general medical care of such patients not a little can be achieved by psychiatric methods In the early stages where there is much anxiety and depression too energetic physical investigation and treatment may do harm reassurance and sedation can do much good The less said to the patients about

their blood pressure and their arteries the better They should keep at work and in their accustomed surroundings as long as they can, unless an acute phase of the illness or depression intervene Emotional upsets oftener aggravate their condition than physical ones so they should be *cushioned against such jolts* Their depression may necessitate hospital care especially because of the risk of suicide or because they are too irritable and neglectful to be *at home any longer* *If there be dementia* even of mild degree, the patient will probably remain in a mental hospital once he has gone there It is, however, not easy to be sure about *mild dementia being present*, it can be counterfeited by passing disturbances *e g* emotional ones

3 HUNTINGTON S CHOREA (see p 1519)

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

Only the mental symptoms will be described here Hypochondriacal and depressive reactions sometimes *follow* infection or the risk of infection such psychogenic illnesses do not belong under this rubric *occasionally* however a patient s *anxiety lest he be developing neuro syphilis turns out to be justified* A syphilitic neurasthenia can occur in the early stages of the disease due to a mild meningitis The *more severe meningo encephalitis—cerebral lues—may be accompanied by* disturbance of consciousness, even to the point of delirium or mild dementia loss of initiative euphoria or *moroseness poor judgement* and impaired memory may persist and the patient be aware of them in greater measure than he is in general paralysis These conditions are often complicated by the signs of premature arterial degeneration in the brain The psychoses that accompany tabes are due to syphilitic changes in the brain often complicated by alcohol trauma heart and kidney disease and other exogenous factors there are also depressive hypochondriacal reactions to the pains and other disabilities which the patient suffers

General Paralysis of the Insane —Dementia is the constant sign of this mental picture, the old descriptions of a 'classical' course with an expansive onset are fallacious but general dementia is almost certain to occur in every case that is not treated All the other symptoms are either neurological and focal, or due to the patient s constitutional predisposition *and previous experiences*

The dementia may at first be quite undetectable as such because it appears under *the deceptive guise of a neurasthenia melancholia or mania* only gradually does the intellectual impairment become manifest In the beginning of general paralysis which is *seldom* abrupt (though it may need a careful enquiry to verify the prodromal symptoms) functional syndromes can be so typical and organic changes so slight that the most expert psychiatrist is misled only by physical and serological examinations can he avoid a blunder A faint degradation of personality a *lapse* in social refinements may be the first indication of *what is wrong* Then *memory for* the events of yesterday and last week becomes less trustworthy what seemed *at first* a trivial absence of mind becomes serious incapacity and yet the patient remains serene and outwardly indifferent to his lapses As *in senile* and *arteriosclerotic* dementia, he may be all right so long as he is in an accustomed rut, but a holiday or a change *reveals his infirmity* His *mood* and interests as the illness goes on become dull or labile, his rages are fleeting his activities fussy if however he is in a manic excitement, with little dementia as yet the affective changes can be violent *and indeed* dangerous just as in a depressive phase the patient may kill himself *Sleepy and slow*, careless about social usages inattentive and ignorant of what he once knew well the more demented patient cannot escape recognition as having an *organic cerebral* affection Elementary problems in arithmetic and questions of general information are more than he can cope with He gives easy *assurances* that he can do them or

puts his questioner off with airy explanations (*e g* that he has not had his spectacles by him lately) when pressed he makes bad mistakes or becomes angry The extent of his failure will of course depend not only on his dementia but on his previous intelligence and habits (*e g* a bank manager retains the capacity to do mental arithmetic when much else has gone) Inability to receive new impressions and to relate them to earlier memories co operates with impaired judgement to give a gross but patchy and fluctuating amnesia Because of these disturbances and especially the bad judgement patients may commit offences ruin themselves by grotesque extravagance and brush aside facts that stare them in the face They will put up with restrictions on their freedom forgetting their protests soon after making them silly reasons are sufficient for their compliance and a tactfully offered cigarette or joke may divert their thought and feeling from some serious matter that angers them Their delusions are due to the same disorders of memory and judgement coloured by their general personality sometimes they are confabulations rationalisations for their having forgotten or spoilt something If the patient had in health tendencies to euphoria and expansive behaviour grandiose delusions and boasting will be to the fore It is however not uncommon to find a fatuous euphoria though there had not previously been affective swings and hypomania in such patients one finds abundant proof of gross impairment of judgement especially shown as defective insight The most advanced dementia appears as a helpless vegetative bedridden state sometimes accompanied by gross focal symptoms such as aphasia and agnosia The physical symptoms (see p 1455) are much intermingled with the mental ones as in the patient s clumsy movements and disturbed speech and handwriting thus in his writing he leaves out letters syllables and words repeats and transposes them messes the paper with blots and sputters writes across the lines puts in meaningless strokes and leaves his mistakes uncorrected the tremulous script shows interruptions in the usual smooth alternation and tempo of movement the letters are of very uneven size and ill spaced Articulatory and aphasic disturbances may affect the sense intonation timbre rhythm and precision of utterance they must not be evaluated in diagnosis any more than the writing disorder may without regard to the patient s previous normal script and speech and the circumstances under which he was writing or talking since people habitually untidy in their enunciation or handwriting can exhibit many of these symptoms when tired or in a hurry

Besides the above atypical mental pictures may be seen either ordinarily or as the outcome of treatment with artificial fever Paranoid states hallucinosi a Korsakoff syndrome epileptiform excitement hysterical disorders and catatonic symptoms of every kind (except flexibilitas cerea) may occur Hallucinations are uncommon except during fever or after malarial treatment in the latter case they are often of paranoid colouring Not the expansive form but a simple progressive dementia is by far the commonest clinical picture depressive confusional and hyperkinetic states are almost as frequent as the expansive

In the Lissauer form the slowness of the dementia is remarkable in comparison with the conspicuous focal symptoms such as the seizures without convulsions or loss of consciousness

The effects of treatment upon the mental state are of great social moment In many patients who do well the personality has the edge taken off it there may be less initiative and force in mental activity and emotion may be less controlled especially in the proneness to anger or to frivolous levity yet the patient is able to return to his former work even though it is responsible and complex he could scarcely however except in the most favourable cases learn a new job or adapt to new and exacting situations

In the *juvenile* form there may be premonitory symptoms of excitability grizzling timidity and backwardness at school Gradually the symptoms of dementia become plain and if the onset be early enough symptoms usually found in severe

mental deficiency naturally appear such as rhythmic or iterative movements grimaces repetitive chewing and sucking of an automatic kind great restlessness and screaming attacks Simple dementia is the usual form, grandiose ideas are exceptional If the illness begins before the age of 10 or 11 years, speech and writing may be completely lost or reduced to a senseless smattering

For *prognosis* and *treatment* see pp 221 and 1458

OTHER CEREBRAL DISEASES

LETHARGIC ENCEPHALITIS —The mental disturbance of the acute attack may merge into a hyperkinetic excitement, with choreiform and athetoid movements insomnia generalised pains mild delirium and occasionally, catatonic symptoms this seldom lasts more than a few weeks There may be subsequently a neurasthenic fatigue and irritability with headaches and poor sleep The distinction between what is neurological and what is psychiatric in the symptoms could scarcely ever be more difficult than in this disease The motor disturbances such as oculogyric crises are not merely responsive to emotional and other psychogenic influences they are inseparable from concomitant mental happenings (*e g* the surging up of anxiety or obsessions) and whole patterns of complicated behaviour *e g* breathing may be involved The motor rigidity of the patient s Parkinsonian state may be paralleled by a lack of the normal drive and fluidity of thought or behaviour Memory however and grasp are unaffected The obsessional symptoms sometimes occur quite apart from oculogyric crises and may greatly distress the patient Depressive phases may result in suicide which is fostered as it were by the keen appreciation which many patients have of their ruined careers and their almost imbecile appearance, so different from what they were and indeed from what they still know themselves to be Paranoid and especially schizophrenic symptoms may develop in the later stages

The younger the patient the more likely is it that he will develop disagreeable anomalies of personality and have attacks of restlessness or even be permanently restless Many children and adolescents after their acute attack become social problems they play stupid or cruel tricks they set every one they can by the ears they may steal behave sexually in an outrageous way or accuse others of sexual offences against them Their activity is not always purposive nor always antisocial they make the same impression as a monkey might who is sometimes mischievous but always on the move There may be no Parkinsonism in these cases The prognosis is not good and they almost always do better when subjected to the *régime* of an appropriate institution they do badly at home or in places where what may be termed normal delinquents and social problems are cared for

SYDENHAM S CHOREA —The usual mental changes here are lability of affect and irritability These are seen as naughtiness outbursts of anger or crying resentment at sudden noise or light in others there is lessened spontaneity often masked by the choreic movements In more severe cases especially in older children these changes are accentuated in the fleeting phases of anger or terror there may be slight delusional trends Still more severe forms with delirium hallucinations delusions of persecution and much excitement are seen in adults *e g* in chorea gravidarum

The tics and compulsive utterances (Gilles de la Tourette s syndrome) which may follow chorea are evidence of the interplay between hereditary psychic and structural factors Chorea is more prone to occur in those whose families show nervous disorders especially schizophrenia The motor after effects especially tics appear and disappear under emotional influences they are also conditioned by the original choreic disturbance of neuromuscular function The obscene ejaculations of la Tourette s syndrome are dependent on much the same articulatory and respiratory hyperkinesias as are the breathing spasms of encephalitis *lethargica* though

they are also dependent on psychological tendencies and experiences They illustrate how psychological influences work through available bodily structures and functions, whether morbid or healthy The obsessional element in this affection is comparable to that in encephalitis lethargica

DISSEMINATED SCLEROSIS —Slight deviations from mental health are frequent but obvious ones rare in this disease Affective lability may be conjoined with a slight disorder of judgement so that a baseless euphoria develops but this is not universal and many of the patients are depressed Acute outbursts of excitement, hallucinosis or delirium occur in a few cases and dementia in the advanced stages The most important mental disorder in them is that which appears as hysteria A hysterical personality has not been present in these patients before the disease began and the symptoms are in that respect only dubiously hysterical they do however in other respects conform in that they can be evoked psychologically and removed psychologically they may centre on and elaborate actual anomalies *e g* of movement or sensation and may still yield to hypnosis or other psychological measures They can greatly confuse the diagnosis

SCHILDER S DISEASE —In this disease profound dementia gradually develops along with the blindness deafness aphasia and agnosia and other focal symptoms In the juvenile cases there may be at first disturbances of behaviour like those of juvenile encephalitis lethargica

PARALYSIS AGITANS —This may be accompanied by hypochondriacal depression Sometimes this is an expression of the cerebral disease which also causes the Parkinsonism, and in that case the prognosis is bad sometimes it is a recurrence of depressive attacks which have occurred at times of stress earlier in the patient s life and then the outlook is fairly favourable Senile dementia is of course not infrequent in these elderly patients

CEREBRAL TUMOUR —Apart from any aphasia and apraxia the mental state here is more closely related to general intracranial tension than to any local disturbance The size and rate of growth of the tumour are therefore important in this regard If rapidly growing there is more disturbance of consciousness with impaired memory disorientation incoherence and sometimes hallucinations and confabulation this clouding of the mind fluctuates a good deal In more slowly growing tumours lucidity is preserved and change of disposition is the prominent feature The patient s earlier tendencies get freer play unsuspected ones appear and a series of foolish investments for example or homosexual escapades may for years divert attention from the organic disease The moria or fatuous wit and cheerfulness often attributed to frontal tumours but also found in other cerebral diseases may give the impression of being a hysterical pseudo dementia other apparently psychogenic symptoms may prove misleading A straightforward depressive attack can occur or indeed any functional syndrome

Hallucinations may depend on a focal lesion as in the cases in which they are limited to the hemianopic field or are solely of taste and smell

CEREBRAL ABSCESS —*The mental symptoms are those of tumour with or without* others due to meningitis

ACUTE MENINGITIS —There may be delirium preceded during the prodromal stage by irritable apathy and followed by months of moody neurasthenia

CEREBRAL TRAUMA —After concussion there is commonly retrograde amnesia and there may be later also amnesia for events following the injury the extent of this depends on the severity of the damage Delirium may ensue it has little that is characteristic and is more frequent in alcoholic and elderly people A Korsakoff syndrome may develop Twilight states are rather more common during them acts of violence may be committed as in epilepsy and afterwards quite forgotten Traumatic epilepsy may follow The later changes in personality are commonly those that may be found lingering after any toxic or other structural impairment of

the brain But sometimes the disturbance of consciousness is more persistent the intellectual damage greater, the deterioration progressive, in such cases there is usually cerebral arterial disease an unrecognised alcoholism cerebral tumour general paralysis of the insane or some other complicating factor In predisposed persons the cranial injury may be responsible for a melancholic attack, schizophrenia or other functional ' syndrome the prognosis is usually good even if the illness lasts many months

Minor symptoms which may be hysterical occur frequently after cerebral trauma This is partly because of the site of the injury which favours vague physiogenic symptoms that respond readily to emotional and other psychological influences Many of these symptoms are, however, produced by psychical rather than physical mechanisms Not injured cells, but mental attitudes are at the bottom of the tremblings faintings, weakness, paræsthesiæ and other troubles so often the sequel of a trauma in itself little likely to have such effects They are not responses to the actual injury, but to the situation created by the injury It is as unwise to dub all such vague post traumatic phenomena hysterical as to attribute them entirely to the direct injury If there is slight amnesia of the typical kind with difficulty in concentration and head ache it is fairly probable that these are physiogenic residues if there has been an interval between the actual concussion and the appearance of the indeterminate symptoms a history of psychopathic predisposition and an adequate psychogenesis (*e g* economic fears and insecurity or claims for compensation with repeated medical examinations and patent uncertainty among the experts) the condition is likely to be neurotic Much will of course, depend on the neurological and other findings including the demonstration of localised lesions, thus damage to the frontal lobes may much change the personality and in other sites be responsible for an apraxia say or a visual defect Too rigid and doctrinaire an insistence on discriminating neurogenic from psychogenic residues of the injury can be harmful the main matter is to prevent neurotic attitudes and symptoms from developing or if already there from continuing

The degree of intellectual impairment can sometimes be measured and the de parture from normality demonstrated by psychometric methods (see p 1694) Among the tests employed those which require a capacity to deal with abstract con cepts (*e g* sorting objects according to qualities they have in common) are particularly informative

EPILEPSY —Although the motor seizure is the chief symptom of epilepsy and the decisive one in diagnosis there are minor or equivalent symptoms as well as delirium twilight states and dementia to be included among the mental disorders of this illness

Instead of a major fit the patient may become unconscious or he may pass into a twilight state in which for a few minutes or longer he wanders about in a dazed way and does inappropriate things having afterwards complete amnesia for all this, or there may be a sudden interruption of action and speech during which the patient remains immobile or makes some automatic or aimless movements Epileptic furor is a delirious state in which acts of violence may be committed it lasts often for several days is accompanied by disorientation and hallucinosis and is much rarer than is popularly or forensically suppo ed All the states of disturbed consciousness mentioned above are most often seen as equivalents for a seizure the twilight states, however, may precede the motor attack follow it, or be accompanied by a few violent clonic movements

Apart from their seizures epileptics are prone to swings of mood—towards anger shallow sentimentalism or depression—which may pass over into a fugue during which the patient wanders a long way from home

The likelihood of dementia later cannot be inferred from the symptoms of the epilepsy except that it is greater if attacks occur very often *Apparent* dementia may be the result of intoxication with anticonvulsant drugs or of the idleness and sterile

life in an institution When there is genuine dementia it begins as a faint loss of interest and concentration with increased sensitiveness to supposed slights then memory falls off somewhat the trivial and the important are muddled together and the patient talks with much circumlocution he is fond of needless system assumes and parades virtues he has not *e g* an intellectual bias or a devout spirit and is child ishly pleased when anyone praises him Later a profound dementia may supervene but this is not common it is unlikely that the changes of character just described are part of a dementing process many epileptics who exhibit some of the most disagreeable features of this sort never become plainly demented and many severe epileptics are free not only from dementia but also from these traits There is ground for regarding this impulsive pretentious fawning and snarling way of some epileptics as partly a variable expression of their constitutional predisposition (to which the motor seizures are likewise due) and partly as a reaction to their situation Consequently it is much less evident or not evident at all in those who in spite of their fits live comparatively normal lives

MIGRAINE —Occasionally sharp changes of mood behaviour and personality may take the place of the ordinary attack with headache It has often been observed that emotional stress may precipitate an attack and psychological guidance which im proves emotional stability has been found to lessen the frequency and severity of attacks in many patients

INTOXICATIONS

1 ALCOHOLIC DISORDERS

Alcohol is so permissible and trusted a poison so easy of access for those who wish *to escape from their troubles that it is resorted to in excess by maladjusted* persons consequently its effects may complicate or be complicated by the psycho pathic anomaly which favoured the taking of the drug *e g* episodic excitement or depression anxiety cerebral arterial disease paranoid states hysteria The acute effects of a single dose of alcohol are either the well known phenomena of intoxication or an excitement (*mania a potu*) sometimes with clouding of consciousness The excitement is commoner in people with cerebral trauma arterio sclerosis epilepsy or unstable hysterical personality and in them may lead to acts of violence rarely it may occur in normal persons who have taken alcohol when they were exhausted or upset

In chronic drunkards a dementing *demoralisation* can occur Their narrowing of interest superficiality of thought weakness of memory and moral decrepitude are reminiscent of what happens in many epileptics and some early general paralytics The crudeness and even brutality of their conduct is in ill accord with their maudlin prating about virtues and their pot house jollity The mood of these men can be as labile as their abandonment to it is constant they pass from rage to weeping and laugh soon after with no shame for themselves and no thought for the miseries they put on their families Such degradation is of course far from being the rule some chronic alcoholics become only cheap editions of themselves with their former qualities underlined or smudged rather than defaced they are perhaps weak and irritable untrustworthy or lying but not given to savage fury, nor grossly damaged in judgement and social feeling Some of them develop delusions especially of jealousy They collect as paranoid people of other kinds do scraps of alleged evidence which they piece together to prove their suspicions right complicated delusions of persecution however they rarely develop Sometimes the delusions of jealousy fade as the patient gets more and more facile but more often they persist as a chronic insanity and are of the greatest danger to the suspected wife murder is not unknown in such cases

The nature of the delusions is to be attributed in part to the lessened sexual potency of chronic drunkards and to the domestic wretchedness and aversion they often create as well as to the same causes as in "functional paranoid states where such delusions are also common, especially in middle life

The symptoms of *delirium tremens* would appear to differ in nothing but severity from the essential symptoms of any delirium (see pp 1625 1639) Some observers however, deny this The anxiety amounts to terror, mixed oddly enough with euphoria, optic and cutaneous hallucinations are vivid and restlessness can be extreme There is almost complete sleeplessness and much disorientation as to time and place, but not as to personal identity The patient s attention wavers between *his hallucinated and his actual surroundings* but can usually be caught and held for a few moments He is very suggestible, as most chronic drunkards are pressing on *his eyeballs for example will very likely make him see whatever one tells him he* sees and he will read aloud from a blank sheet if one wants him to Among the visual hallucinations *may be miniature ones (micropsia) and many illusional percep*tions The content of the hallucinations changes rapidly and a false perception in one field *(e g a vestibular one) tends to evoke others (e g of sight, touch or hearing)* Insight is commonly lacking, afterwards there is patchy amnesia for what has happened in the delirium The death rate, with adequate treatment has been about 1 in 7 and of those who die most of the men are under 40 and most of the women under 45

In *acute alcoholic hallucinosis* auditory hallucinations of a persecutory kind are prominent and consciousness is not notably clouded It is rarer than delirium tremens and is more prone to follow a bout or orgy of drunkenness The patient is frightened, but not obviously out of his mind, he is correctly orientated and may be able to go about his business for days Auditory hallucinations are vivid and insistent after a premonitory phase in which there are sensitiveness to sounds and roaring singing hissing etc in the ears Tormenting voices sharply localised but seldom fastened upon bystanders abuse threaten or discuss the patient they may say his wife plays him false order him to kill himself describe his every movement especially at private moments in the bath or lavatory cast up his more shameful secrets at him shout his thoughts aloud There may be many voices of men *women and children* all talking together and perhaps rising and falling in the same rhythm as his pulse *They are so real that the patient answers them he may be in doubt* about the presence of his tormentors and may shout back insults to see if a blow will follow from the *owners of these evasive pursuing voices Hallucinations of sight* and other senses are far less prominent than those of hearing cutaneous ones *e g* of being sprayed with a cold liquid are not uncommon Delusions are usually inconspicuous they are, as a rule attempts to account for the hallucinations and they commonly fade out of the picture or pass into a chronic persecutory disorder Flight or acts of violence may result from the patient s fear or anger Usually it is a matter of only 2 or 3 weeks before the hallucinosis clears up if no further alcohol be drunk sometimes however a delusional state more rarely a Korsakoff picture supervenes in predisposed persons After recovery there is little or no amnesia for the events of the hallucinosis Relapse is to be feared if the drinking goes on

The *Korsakoff* syndrome is not invariably associated with polyneuritis Nor as stated on p 1627 is it limited to alcoholism *it can follow other* severe chemical and mechanical injuries to the brain In alcoholics it is commoner in middle life developing either *insidiously in the course of chronic* alcoholic demoralisation, or after delirium tremens women are especially prone to develop this syndrome after *the delirium* The symptoms have already been described The disorientation superficial appearance of clarity incapacity for initial perception and subsequent recall (extending often to most of the material of memory) yet with retention of some capacity for learning by repetition along with confabulation *dullness of emotion*

and initiative and grossly impaired judgement making a striking picture Complete recovery is on the whole uncommon occurring in less than a quarter of all cases The mortality rate is higher in women and older people in those with acute onset and with a red cell count below 3 000 000 or with a rise in the protein content of the C S F It does not correlate with the severity of the peripheral neuritis

Chronic delusional states have been referred to above they are sometimes called alcoholic paranoia but inappropriately so jealousy is the commonest and most dangerous feature Alcoholic epilepsy has been described It is a symptomatic epilepsy often atypical sometimes in unstable hysterical patients it may be brought about through overbreathing when intoxicated

Diagnosis—The diagnosis of alcoholic psychoses must depend much more on a history of drunkenness in any patient than on his clinical psychiatric features none of which are limited to alcoholic disorder Since however alcohol is far the commonest cause of most of the toxic abnormalities described it can be safely presumed in some cases in which the certain history of addiction is unobtainable

Differential diagnosis so far as ætiology is concerned will turn on somatic findings including the results of chemical tests If the form of the disorder is in question the chief diagnostic difficulty arises with acute hallucinosis and the chronic delusional varieties A hallucinosis of similar type can occur in schizophrenia and in affective disorders but in the latter is recognisable by the ideas of self reproach expressed the differentiation from schizophrenia is difficult since in many of the cases the progress of the disorder is towards a chronic schizophrenic psychosis and one may suppose that in these patients the intoxication had activated as it were the same mechanisms as those involved in schizophrenia or had complicated a schizophrenic illness This applies also to the chronic psychosis with delusions of jealousy There is no value in differentiating carefully the clinical varieties of alcoholic psychoses since they overlap

Treatment—Social prophylaxis is the main thing The incidence of alcoholic psychoses in England is less than a third of what it was 40 years ago and this may be attributed almost entirely to social influences Individual prophylaxis is scarcely to be considered save as a by product of psychiatric treatment since a great proportion of unstable persons are potential drunkards and in any case we cannot yet tell which alcoholics will become mentally ill through their drinking Social prophylaxis is so immeasurably better in forestalling alcoholism and the psychoses and degradation that sometimes spring from alcoholism that deliberate individual prevention is here negligible

When alcoholism is itself to be treated independently of its ill effects upon mental health the problem is that of any drug addiction Absolute removal of the drug is essential in the first place This may be effected for a time by getting the patient into a hospital or home where he cannot obtain the alcohol he desires but to ensure that the patient who has had years of excess shall henceforward be able to put aside alcohol while it is within his reach a great emotional upheaval *e g* bereavement religiou conversion fear of death and considerable changes in his human environment are required These are provided for instance by a semi religious organisation of former drunkards called Alcoholics Anonymous which had its rise in America and which has had notable success in the last decade For the most part treatment of alcoholism without restrictions upon access to the drug is a failure the restrictions must at first be imposed from without not left to the patient s self control and judgement Psychotherapy is a necessary feature of the treatment in the many cases in which inner struggles and neurotic disabilities have been the basis for the addiction it must however be conjoined with vigorous social measures (see pp 1618 1619)

Methods which aim at conditioning the patient to have a distaste for alcohol are sometimes successful The unconditioned reflex of nausea and vomiting (evoked by emetine) is linked up with the sight smell and taste of alcohol Thoroughly

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Prognosis —This is poor as regards recovery from the addiction especially if *the patient s profession makes access to the drug easy The more normal the patient s* personality the better the outlook After apparent cure however relapse is frequent and the outlook is then correspondingly worse unless the patient can be stopped from getting the drug Many morphine addicts also take alcohol cocaine and such other drugs as they can get Suicide with morphine is not uncommon for obvious reasons Death is sometimes the result of cutaneous infections especially when the patient is grossly undernourished

Treatment —This must be in an appropriate institution, general hospitals seldom have the necessary facilities Treatment at home is bound to be a failure It should be impossible for the patient however skilled in stratagems to get hold of morphine He should if possible contract to stay for at least 2 months The withdrawal of the drug should be abrupt and total except in very debilitated patients, tapering off prolongs the distressing period of withdrawal symptoms and gives *opportunity* for the patient to develop psychopathic reactions and *dodges* If the patient s condition demands a gradual withdrawal this need seldom extend over more than a fortnight When an abrupt end has been put to the taking of morphine the rigours of the first 4 or 5 days (after which the worst is over) can be alleviated by sedatives in fairly large doses copious fluids warm baths massage and fresh air gastric lavage and alkalis help and for circulatory symptoms caffeine may be given with small doses of morphine also in very severe cases Insulin in subcoma doses has been used to ease the period of withdrawal After this phase is past sleeplessness may still be intractable in giving sedatives or hypnotics for this barbiturates and paraldehyde with occasional doses of hyoscine are the safest but should be used sparingly with frequent changes and it need hardly be said complete refusal to let the patient know what he is having Psychological treatment is of great importance but there is no specific technique applicable to this addiction To be successful the *psychological* treatment requires the co operation of the patient s *family* as well as of the patient himself who will be well advised to keep in touch with his physician for years The great difficulty of getting the drug in this country because of the vigilance of the Home Office is an immensely favourable factor after active medical treatment has ceased It is wise for the patients to eschew alcohol and of course all hypnotic drugs

3 OTHER INTOXICATIONS

Cocainism and Cannabis addiction are rare in England The causes and symptoms are similar to those of other addictions *e g* alcohol and morphine Deliria hallucinations Korsakoff syndrome or demoralisation can occur in the former conditions microptic and cutaneous hallucinations *e g* of bugs under the skin are prominent A paranoid schizophrenic state sometimes comes on usually clearing up after the drug has been *stopped In treatment what was said of morphinism mostly applies* here though withdrawal symptoms are less severe

Bromide intoxication often passes unrecognised All the organic syndromes can occur usually as complications of a pre existing disorder for which the bromide has been prescribed A delirium and a paranoid confusional state or lachrymose amnesic syndrome are the usual forms In the more long standing and severe forms cachexia circulatory failure and even death may occur Acne and other physical signs of intoxication or idiosyncrasy may not be evident Diagnosis rests on the history and the amount of bromide found in the blood more than 50 mg per 100 ml being indicative of a considerable intake or retention of bromide Treatment consists in complete withdrawal of the drug promotion of its excretion by giving sodium chloride and fluids in large quantities and general physical and psychiatric measures

Barbituric acid derivatives such as barbitone (Veronal) and phenobarbitone (Luminal) can in rare cases lead to apparent euphoric dementia likely to be mistaken

carried out the method has yielded fairly good results, half of those treated are reported as still abstinent 4 years afterwards It is impossible however, to benefit the addict who does not seriously want to stop drinking In a small proportion of chronic alcoholics amphitamine sulphate is said to diminish the craving

A drug which may help the patient s efforts to remain abstinent is disulfiram (Antabuse) taken daily by the mouth this ensures that a drastic reaction will ensue if the patient drinks any alcohol since acetaldehyde is then liberated within the circulatory system Knowledge of this very disagreeable consequence deters the former addict from drinking but he can evade the risk if he wants to by ceasing to take the drug It is *therefore pointless to administer it unless the patient sincerely wishes to be abstinent* The risks of the method and its dependence upon the patient s co operation make it desirable that it should be initiated in hospital and undertaken only as part of a general plan of treatment and rehabilitation

The grosser mental disorders due to alcohol need hospital treatment Delirium tremens should be treated as far as possible without hypnotics which have little effect upon the excitement and sleeplessness unless employed in dangerous doses if any paraldehyde or hyoscine should be used Circulatory failure and accidental self injury are most to be guarded against The continuous bath at body temperature is sometimes beneficial, otherwise the patient should be in bed with a minimum of necessary restraint under the care of an experienced nurse and ensurance of adequate diet—mainly fluids and glucose and large amounts of thiamin or the whole vitamin B complex No alcohol should be given Occasionally lumbar puncture is helpful Insulin and corticotrophin have been found beneficial but the evidence is not impressive

Especial care must be taken against the early discharge from hospital of alcoholics with delusions of jealousy If they have been certified they may add a deep resentment on this score to their other grounds of morbid hatred, and there is grave danger that they may, if they resume drinking attack their wives murderously

2 MORPHINISM

Only the effects of this belong among the organic disorders its causes and the incapacity of the addict to escape from it are due to social and intrinsic factors not *to any physical damage* Weak *unstable unhappy people e g* many homosexuals are most likely to become addicts it is rare to meet an addict who has not shown pronounced psychopathic traits before his addiction began and few of those who profess to have been seduced into the habit by more or less injudicious administration of morphine for some pain they had are in that telling the whole truth Yet it is a wise caution that withholds morphine from all chronic disease *that is not hopelessly* progressive and hesitates to prescribe it at all for those whose personality or opportunities make the risk of addiction greater

Symptoms —These are not at first noteworthy unless the patient be seen during the next 2 or 3 hours after he has taken his drug The symptoms of withdrawal sometimes severe are more likely to occur in those whose tolerance has been raised by the habit they consist of yawning sneezing overflow of tears and saliva fullness in the head then restless movements malaise twitching in the face tremors palpitation *indigestion vomiting diarrhœa strangury*, sleeplessness and circulatory upset which may go on to collapse

It is difficult to judge how far the drug itself is responsible for the demoralisation that is met with in chronic morphine addicts probably as important in causing it are the psychopathic personality of the addict and the underhand life he must lead Laziness and lying are frequent and the patient may resort to subterfuges or even crimes *to get his drug* Dementia does not occur delirium is rare The physical effects of chronic morphinism are dryness of the skin hair and nails constipation and anorexia partial impotence and poor resistance to infection

METABOLIC, ENDOCRINE AND VISCERAL DISEASE

1 METABOLIC DISORDERS

Various metabolic disorders can similarly i e non specifically affect mental health *Diabetes* for example which is especially frequent in families with a pre disposition to affective psychosis may be accompanied by transient phases of depression, anxiety or excitement which correspond to changes in the blood sugar level or a ketosis may be ushered in by mild delirium A diabetic pseudoparesis with peripheral neuritis may cause slight difficulty in diagnosis In children mild hypo glycæmia may be responsible for anxiety naughtiness and other disturbances of behaviour Anomalous psychic states may be produced in the rare condition of hyperinsulinism and be mistaken for hysteria or an anxiety state of the psychogenic sort *Gout* may occur in people predisposed to affective disorder often a depressive phase precedes an attack Alkalosis and anoxæmia may each be the cause of mental disturbance of the organic type In *pernicious anæmia* there may be symptoms e g an acute confusional state referable to the structural changes in the central nervous system but more often depression occurs without organic features mania can also occur and in some cases a chronic paranoid condition The more organic the picture the poorer the prognosis for a return to mental health Of deficiency diseases *pellagra* is the one most commonly productive of mental disorder It must be remembered that a long standing anorexia of psychogenic origin or occurring in the course of a chronic melancholia may itself lead to a pellagroid condition so that the symptoms of mental disorder will then be those of the original illness plus those due to the deficiency The clinical picture is sometimes very like that of hysteria or the usual organic syndromes may be produced especially florid confusion with perhaps hallucinations of fire The nutritional factor in alcoholic psychoses especially Wernicke s encephalopathy is prominent

In the metabolic di orders just mentioned the physical phenomena are relatively coarse and obvious It is in some cases proven and in others highly probable that less obvious metabolic disturbances are among the primary symptoms of functional mental illness or are its pathological basis The acid base equilibrium and the electro lytes of the blood the metabolism of carbohydrate fat and protein and the chemical regulation of the vegetative activities are all in such forms of mental illness as schizophrenia and mania subject to changes which have not as yet been used in the path ology or treatment of these conditions because the findings are not sufficiently constant or specific

2 ENDOCRINE DISORDERS

These play a more prominent role in the investigations than in the clinical practice of psychiatry Many endocrine preparations have it is true been administered to schizophrenic sexually perverted and melancholic patients either empirically or in accordance with a premature and ill devised theory but the good results of all this are negligible Œstrogen treatment of menopausal neuro vegetative symptoms is a rational procedure but the blind use of endocrine substances in psychiatry has had its day

Exophthalmic goitre is more prone to occur in anxious nervous people especially after some sudden shock The usual concomitants—restlessnes tension irritability difficulty of concentration and liability to sudden changes of mood—may be complicated by a definite mania or depression and if the disease be severe or advanced delirium and confusion may supervene Though such organic syndromes mean as a rule a bad prognosi they sometimes clear up dramatically after operation The interaction of constitutional and psychogenic factors with the actual thyrogenic

for general paralysis because of the ataxia tremor articulatory disorder and other neurological signs Recovery is the rule when the drug is stopped Picrotoxin may be needed for acute poisoning For the addiction itself essentially the same problems and methods of treatment are in question as with other drug addiction This applies also to *ether*, *chloral* and *paraldehyde*

Mercury and *lead* poisoning may lead to mental disorder (see pp 368 and 382), *manganese* to a Parkinsonian syndrome with compulsive symptoms (reminiscent of encephalitis lethargica) and a mild paranoid or euphoric dementia, and *benzene* or *carbon disulphide* may cause delirium

Acute carbon monoxide poisoning in rare instances leaves behind severe mental disorder of the amnesic aphasic kind, which may not become apparent until several weeks after the recovery of consciousness More commonly it results in a clinical picture almost indistinguishable from hysteria this may take months to clear up and is in no wise benefited by psychotherapy Chronic poisoning by small quantities of carbon monoxide causes neurasthenia

INFECTIONS AND EXHAUSTIVE DISORDERS

1 INFECTIOUS TOXÆMIAS

Delirium and a Korsakoff syndrome are the more acute, and neurasthenia the milder signs of mental disorder due to an infectious fever In many of the cases however in which mental disorder is attributed to sepsis or other infection either the mental changes are unconnected with the infectious process or there has not been an infectious process as is often found when one enquires into an alleged attack of influenza' and finds it was nothing of the kind There are three possibilities the mental changes are mainly due to the infection they are independent of the infection they are partly due to the infection and partly to other, usually constitutional causes The depression that occurs in and after many infections is usually of the third category mentioned, delirium instances the first possibility, and the second is often exemplified when some non organic syndrome is put down to sepsis *e g* in the tooth sockets

Wherever a delirium or other mental disturbance of one infection differs from that of another *e g* the delirium of typhoid from that of pneumonia the difference lies only in the severity and duration of the physical effects of the intoxication and in the peculiarities of the affected person no mental symptoms specific to any one infection can be demonstrated Among the individual peculiarities just mentioned must be included a constitutional predisposition or readiness to respond with symptomatic psychoses to mainly physical ills

There are a few infections that hardly ever cause mental disturbance *e g* tetanus and diphtheria others do so by their local cerebral incidence *e g* malaria or encephalitis lethargica *Tuberculosis* from its chronicity and its occasional incidence on the central nervous system has a special position Its treatment moreover especially in the pulmonary form necessitates an abnormal unsatisfying life for a time and this with the toxæmia seems to be responsible for euphoric or anxious restlessness in which erotic tendencies and irritability are often prominent Spes phthisica is partly attributable to toxic euphoria in part it is a form of over compensation for fear

2 EXHAUSTION AND INANITION

These especially if conjoined with some shattering experience—an earthquake incessant bombardment a bereavement—bring about severe mental disturbance *e g* a twilight state or a delirium Hæmorrhage and cachexia may be responsible for light headedness as in advanced carcinoma or after a severe operation

METABOLIC, ENDOCRINE AND VISCERAL DISEASE

1 METABOLIC DISORDERS

Various metabolic disorders can similarly, *i e* non specifically affect mental health *Diabetes* for example which is especially frequent in families with a pre disposition to affective psychosis may be accompanied by transient phases of depres sion anxiety or excitement which correspond to changes in the blood sugar level or a ketosis may be ushered in by mild delirium A diabetic pseudoparesis with peripheral neuritis may cause slight difficulty in diagnosis In children mild hypo-glycæmia may be responsible for anxiety naughtiness and other disturbances of behaviour Anomalous psychic states may be produced in the rare condition of hyperinsulinism and be mistaken for hysteria or an anxiety state of the psychogenic sort *Gout* may occur in people predisposed to affective disorder often a depressive phase precedes an attack Alkalosis and anoxæmia may each be the cause of mental disturbance of the organic type In *pernicious anæmia* there may be symptoms *e g* an acute confusional state referable to the structural changes in the central nervous system but more often depression occurs without organic features mania can also occur and in some cases a chronic paranoid condition The more organic the picture the poorer the prognosis for a return to mental health Of deficiency diseases *pellagra* is the one most commonly productive of mental disorder It must be remembered that a long standing anorexia of psychogenic origin or occurring in the course of a chronic melancholia may itself lead to a pellagroid condition so that the symptoms of mental disorder will then be those of the original illness plus those due to the deficiency The clinical picture is sometimes very like that of hysteria or the usual organic syndromes may be produced especially florid confusion with perhaps hallucinations of fire The nutritional factor in alcoholic psychoses especially Wernicke s encephalopathy is prominent

In the metabolic disorders just mentioned the physical phenomena are relatively coarse and obvious It is in some cases proven and in others highly probable that less obvious metabolic disturbances are among the primary symptoms of functional mental illness or are its pathological basis The acid base equilibrium and the electro lytes of the blood the metabolism of carbohydrate fat and protein and the chemical regulation of the vegetative activities are all in such forms of mental illness as schizo-phrenia and mania subject to changes which have not as yet been used in the path-ology or treatment of these conditions because the findings are not sufficiently constant or specific

2 ENDOCRINE DISORDERS

These play a more prominent role in the investigations than in the clinical practice of psychiatry Many endocrine preparations have it is true been administered to schizophrenic sexually perverted and melancholic patients either empirically or in accordance with a premature and ill devised theory but the good results of all this are negligible Œstrogen treatment of menopausal neuro vegetative symptoms is a rational procedure but the blind use of endocrine sub tances in psychiatry has had its day

Exophthalmic goitre is more prone to occur in anxious nervous people especially after some sudden shock The usual concomitants—restlessness tension irritability difficulty of concentration and liability to sudden changes of mood—may be compli cated by a definite mania or depression and if the disease be severe or advanced delirium and confusion may supervene Though such organic syndromes mean as a rule a bad prognosis they sometimes clear up dramatically after operation The interaction of constitutional and psychogenic factors with the actual thyrogenic

intoxication makes some treatment of the anxiety by psychological as well as other methods desirable in many cases of exophthalmic goitre either as a preliminary or supplement to partial thyroidectomy

In adult *myxœdema* the slowing of mental activity may sometimes be accompanied by a chronic paranoid psychosis or there may be a phase of excitement with hallucinations the variety of syndromes that can occur is referable to pre existing constitutional tendencies and to the varying severity and rapidity of development of the thyroid deficiency An apparently 'functional' syndrome *may precede the* overt *myxœdema*

Juvenile and congenital myxœdema are described elsewhere (see p 496)

Tetany may be signalised by epileptiform seizures or there may be a proneness to psychogenic fits thus the patient may spontaneously overbreathe until a convulsion is induced *Hysterics sometimes* use hyperventilation in this way In severe tetany a resistive lethargy or an excited incoherent confusion may occur

Pituitary diseases are more often accompanied by mental symptoms that are a comprehensible *reaction to the* physical symptoms than by organic syndromes, the latter when they occur may be due to increased intracranial tension In acromegaly depression reserve touchiness and irritability are not surprising though some acromegalics remain cheerful as long as their disabilities are moderate and sometimes there is a blindness to the disease a lack of insight even when it is advanced In dystrophia adiposo *genitalis a rather childish* placidity may be met In adiposis *dolorosa depression may be severe or hysterical symptoms may develop Simmonds s* disease may be accompanied by depression severe anorexia reaction to the psychosexual disturbance and in the later phases by organic syndromes due to the cachexia Similarly, disorders of pituitary function have been found in some cases of anorexia nervosa In Cushing s basophil syndrome depression and other mental disturbances can occur

Addison s disease is accompanied by a neurasthenia of which for a time the physical basis may be quite overlooked (as may also occur in myasthenia gravis), *in the later* stages delirium has been known to occur

Acute anxiety attacks may occur from a phæochromocytoma Some persons during the course of treatment with cortisone or corticotrophin develop an acute psychosis which clears up if the drug is withdrawn

Sexual epochs may in women be associated with mental disorder of the organic type *e g* some psychoses of pregnancy and the puerperium During pregnancy plain psychosis is rare, but hysterical symptoms depression and anxiety *are fairly* common, especially if the mother is reluctant to have another baby a gross psychosis may however, break out during the latter months of pregnancy The organic mental syndromes may develop along with polyneuritis eclampsia or chorea gravidarum Termination of the pregnancy is called for on account of the mental condition when there are symptoms of organic psychosis which are likely to get worse a history of suicidal attempts or infanticide in connection with previous pregnancies and a depression again in this one or if on other grounds there is a *clear risk of suicide or* other untoward result of the mental illness should pregnancy continue The decision is often a very difficult one requiring an expert knowledge of psychiatry for the careful appraisal of ætiology and prognosis essential in every case The question must turn mainly on the therapeutic value of terminating the pregnancy so far as the mother s mental state is concerned as well as upon the stage of pregnancy reached

In the puerperium 'functional' psychoses often develop in predisposed women if there be septicæmia as well a confusional state or a delirium *followed by a period* of neurasthenia may occur In many cases the delirious puerperal psychosis clears up in a week or two the more endogenous varieties have sometimes a less satisfactory outcome than their form and onset suggest Infanticide may occur in a puerperal psychosis especially if the mother has while pregnant felt resentful at

having a baby or been troubled by murderous preoccupations *e g* obsessions Psychoses of lactation are rare and seldom of the organic type Menstruation is apt to be associated with depression irritability and languor in many women especially during the few days before the period begins there are no menstrual psychoses but the liability to suicide and to psychopathic reactions is somewhat higher at this time There is no satisfactory evidence that the affective disorders of later middle life (involutional melancholia ') are caused by the endocrine changes of the menopause they are certainly not benefited by œstrogen therapy Puberty and the climacteric are periods of stress during which schizophrenic and affective disorders may occur The effects of castration are dependent on the age at which the gonads are removed intellectual development is unaffected but the emotional and conative activities of those castrated in adult life may be impaired Neurasthenic symptoms are frequent and in women anxiety symptoms may appear

3 VISCERAL DISEASE

This may be directly responsible for mental disorder of the organic type Thus *cardiac* disorders predispose to an anxiety which at night may take the form of mild delirium with restlessness terror disorientation and auditory and sometimes visual hallucinations With improvement in the circulation the mental symptoms disappear or remain only as a moody unrest Reference has already been made to arterial hypertension (see p 1630) The connection between *alimentary* disorders and neurasthenic states is well attested and is striking in children Jaundice may be accompanied by severe depression but seldom leads to delirium save in the case of acute yellow atrophy *Uræmia* may disturb consciousness greatly in the form of any of the organic syndromes from a twilight state to a euphoric dementia, a Korsakoff condition can occur but is infrequent

The psychological causes or accompaniments of many visceral diseases have been diligently studied and the conditions in which they appear prominent are sometimes called psycho somatic The problems raised are intricate and the interplay between the physiological and the psychological aspects of the disease processes has not as yet been fully disclosed in any of the major conditions studied *e g* ulcerative colitis peptic ulcer bronchial asthma

AFFECTIVE DISORDER

This is of three types

1 Manic excitement and hypomania
2 Melancholia and mild or neurasthenic depression
3 Agitated depression and anxiety state

There is in each case a major and a minor form Each is related to a more or less characteristic personality and for each the cause of occurrence may be chiefly environmental or chiefly hereditary Combinations are frequent (mixed forms) or there may be successive appearance of the different types often with an interval between the attacks A benign outcome or periodic course is the rule for the major forms but not for the minor which often tend to become chronic This is partly because the environment can have more influence whether for good or bad on the course of the minor than of the major more explosive and sweeping forms It would be a very convenient thing if endogenous cases could be sharply differentiated from psychogenic ones as in the Kraepelinian scheme but it cannot be done

Ætiology —INTRINSIC —Heredity is the most constant single cause Research has been mainly into the major manic depressive cases The genetic factor is weakly

dominant It may be that more than one gene is concerned but this is hard to tell, because the predisposition to an affective disorder may be latent in persons who have not been subjected to the stresses that would make it manifest, and consequently the usual Mendelian figures are not to be expected The present state of knowledge is illustrated by studies on manic depressive twins among whom 69 per cent of those monozygotic (*i e* with identical heredity) were alike affected with the disorder while the corresponding figure was only 16 per cent for the dizygotic pairs (*i e* with dis similar heredity) In the 31 per cent of monozygotic twin pairs who were not alike in respect of mental illness, the difference must have lain in the environment thus showing the relative importance of external factors in causing the inherited tendency to become manifest Although not manifest as illness the inherited tendency may express itself in bodily and mental constitution

The bodily habit that is found in a majority (not the overwhelming majority) of those with affective psychoses is called pyknic or eurymorph It is best seen in men after the age of 30 It is characterised by large visceral cavities (head thorax, belly) a tendency to fat on the trunk slender shoulder girdle and extremities stocky build a broad face on a short massive neck thick receding hair and later, baldness venules on the cheeks and a disposition to arthritis gout diabetes and especially arterio sclerosis As this John Bull build is so common in mentally healthy people it cannot be regarded as a precursor of mental illness but only as an indication that some of the constitutional and genetic causes or biological requirements for affective psychoses are present

The same is true of the mental constitution or personality Here there are several groups shading off on the one side by way of cyclothymia and other intermediate forms of mild disorder into definite affective psychosis and on the other into normal and stable personality There are those with a pervading gloominess pessimism and feeling of insufficiency that spoils their lives others who are for ever anxious keyed up wondering whether something has gone wrong or will go wrong and whether it is their fault—careworn worrying creatures while a third group is made up of the lively enterprising confident sociable people whose euphoria is patent Irritability may be found in any of these groups especially the second and the last Contrasted or different features are often found mixed in the same patient The most striking characteristic of the personality of manic depressive patients is their ready responsive ness and lability of mood they fluctuate with their surroundings and in many in stances pass suddenly and with small occasion from one mood into another far removed from it

The signs of affective illness may appear in childhood though major outbreaks of mania depression or agitation are rare before puberty When these occur the phases are usually brief and the environmental influences strong Milder forms are often regarded as normal since night terrors and other fears mischievous gaiety and sulky gloom are all familiar enough in children it is the degree occasion and persistence of the affect which must decide whether it is morbid

The psychological crises of puberty are only occasionally affective—chiefly self reproachful depression or agitation—but during adolescence the illness becomes more frequent it seldom however calls for mental hospital care Each menstrual period may be accompanied by *depression or restlessness usually coming* on about 2 days before the period In the third decade of life the number of cases steadily rises and there is another peak in frequency between the ages of 45 and 55 The latter in volutional cases show the influence of age strikingly so much so that they are often *considered as separate disorders*

There is little to choose between the curves of age incidence for morbid depression and morbid anxiety of whatever degree for mania the frequency is highest before the age of 30 as also for affective illnesses with a strong confusional flavour Preg nancy is frequently accompanied by depression and agitation psychological factors

are mainly responsible After childbirth though there be no septicæmia affective illness can occur running a typical and often lengthy course

The female climacteric is a time when anxiety usually mounts and is accepted as an ineluctable effect of the change It may become definite illness persisting even for 2 or 3 years It is doubtful whether there is a specific connection between the endocrine causes of the menopause and so called climacteric insanity the melancholia then coming on is like the melancholia of 5 or 10 years later or the melancholia of middle aged and elderly men in whom the endocrine changes are not the same The influence of sex as a whole is obscure Women have this illness more than men though the manic form is relatively more frequent in men The reactivity is often greater and the syndrome less clear cut in women

There are geographical differences sometimes thought to be racial in the incidence but the little that is known points to environmental rather than intrinsic causes for this It has been suggested that affective psychoses are commonly linked with high intellectual gifts another says they have affinity with mental defect The former statement has better support than the latter but both probably are fallacies depending on the material selected for study

EXTRINSIC —*Physical* —Chronic toxæmia and acute infections especially influenza and pneumonia can be responsible for the illness Various drugs help to heighten the anxiety to a morbid degree *e g* alcohol in certain circumstances insulin or hyoscine Cerebral trauma may provoke an attack The list of physical factors could be much added to but it must be borne in mind that wherever a distinctive rather than incidental physical cause can be found the condition passes over into the category of organic psychoses The most difficult cases in practice are those in which there is a question of cerebral arterio sclerosis or exophthalmic goitre the affective disorders indisputably due to these two diseases may be quite indistinguishable from others for which there is no such organic basis The problem here is clinical rather than fundamental since vascular cerebral endocrine and autonomic functions are particularly concerned in the mechanism of emotional change certain disturbances of the physical apparatus will necessarily be accompanied by many of the psychological phenomena of these emotional changes The depression of paralysis agitans and the anxiety of coronary disease are of the same order The notion that coitus interruptus and other sexual practices produce anxiety is unfounded but they may contribute to it by psychological means

Psychical —A recent misfortune commonplace or tragic may be the cause Any calamity to which human beings are liable may provoke an affective breakdown Sometimes it is induced by the insanity of a close relative However trivial it seems to outsiders the event that has precipitated an affective attack has been felt as a catastrophe by the patient there are no records of great and sudden happiness causing an affective psychosis The nearest approach to a specific connection between the precipitating happening and the type of affective illness is seen in the anxiety disorders which follow a terrifying experience such as exposure to shell fire and bombardment from the air morbid depression following bereavement financial setbacks or degradation is an understandable response it is true but to ascribe the type of response directly to the nature of the experience is specious since on another occasion it may be with hilarious mania that the calamity is met

Moreover the experiences of a lifetime will have determined what calamities are most felt they need not be calamities in other people s eyes at all Experiences spread over years are the common extrinsic cause of the more chronic neurotic forms of affective illness this applies least to chronic hypomania In these chronic conditions the patient s own behaviour has so much to do with what happens to him as it were from outside that to separate extrinsic from intrinsic is very hard

Pathology —The *physiological* changes are characteristic only of emotional disturbance not of morbid emotional disturbance and therefore they are not of

diagnostic value They consist in lability of blood pressure and pulse rate abnormal motility of plain muscle especially *in the alimentary tract* carbohydrate disturbances variations in either direction of the rates of salivary and other secretions and decreased psychogalvanic activity The changes are variable from patient to patient and are not always discoverable More significant are changes in basal metabolism weight sleep and menstruation loss of weight is the rule during the illness Irregularity of menses and then amenorrhœa often occur Rise in the blood iodine content changes in the K/Ca ratio diminished cellular respiration hypercholesterinæmia and signs of adreno cortical hyperactivity have been alleged but not conclusively

The *psychological* changes, in spite of great external differences have the following in common the morbid phenomena are in accordance with the prevailing mood, though not wholly derivable *from it thought is less purposively directed to im* personal ends than it would normally be, but more purposively to personal ones there is a small number of topics of preoccupation in each patient but his ways of arranging and embellishing them can be many the whole body (or parts of it) often receives much of the patient s attention because of more or it may be less feeling in it (hypochondria depersonalisation) misconstructions abound with consequent ideas of self reference and persecution as well as misidentification and there is a feeling of inner tension unrest and excitement however apathetic or carefree the patient s demeanour

The seemingly greater quickness and capacity of manic patients has not been confirmed by psychomotor, intellectual and association tests *hypomanic patients* sometimes however, do better than in their normal state This can be compared to the effects of increasing doses of alcohol Patients with affective disorder are more irritable and excitable than is normal Time appreciation may be grossly disturbed personal time seems to pass very differently from clock time time may seem to stand still, no future is conceivable Perplexity may be conspicuous and explanations of this in terms of Gestalt psychology conditioned reflexes and toxæmia have been proffered

The effects of experience in bringing about this illness cannot be explained in terms of a logical and coherent system unless one accepts the premises of that system and infers what cannot be observed Consequently as there are several such psychological systems there are several explanations They state the conjectured ways in which instinctual energy or libido may become misdirected because of environmental conditioning frustration and loss

Symptoms —SYMPTOMS OF EXCITEMENT (MANIA) —*There is excitability of mood* and movement The *mood* is mostly one of jollity rather infectious but likely to become boring or overbearing, occasionally it turns to anger and resentment It is labile tears will flow readily on some trivial occasion to pass into laughter in a twinkling

Thinking is apparently rapid There is flight of ideas with successive words and phrases *loosely connected only by similarities of* sound or chance associations Consequently the patient wanders from the point whether he can *come back to it* depends on the severity of his condition Jokes self praise flighty comment on his surroundings and facile optimism make up the tenor of his exuberant conversation *Nevertheless the number of topics* he touches on in the course of the day is often more limited than if he were in normal health he reverts to a few matters over and over He may criticise himself with cynical bitterness or humour as he criticises others he may talk a lot about bodily disturbances *e g* his varicose veins or his sore throat His mood and expression are consonant *with what he says* He is distractable herein seeming at the mercy of his sensations and of every small detail whether it be inside himself or as is more common connected with things about him *Judgement is impaired*

Delusions are less common than *distortions* and misstatements People are wilfully

called out of their names events misrepresented bodily sensations exaggerated and accusations of ill treatment or persecution irresponsibly preferred and sometimes long persisted in The more confused and excited the patient the more likely to be deluded and even hallucinated Most of the seeming hallucinations are *façons de parler* or illusions sometimes the patient is as it were pretending or acting the part of a hallucinated person

Activity is exaggerated and in severe cases incessant Its object may change from moment to moment but sometimes the main end is kept pertinaciously in view The patient if tactlessly thwarted gets angry sulky or violent He feels very strong and seems untiring He has many schemes of an optimistic cast and in the course of putting them into action may be extravagant inconsiderate or interfering Sexual excesses or drunkenness may occur and bring much harm especially when the patient is a young woman Troubles with the police arise through silly pranks or self confident exploits

Sleep is brief but deep In the early and mild stages the patient looks exceptionally well but after weeks or months of over activity and little sleep he looks exhausted with sordes on his lips, hoarse voice drawn skin and perhaps less total activity but many unfinished little movements Food is welcomed in the mild stages when the activity is great the patient does not give himself time to eat but plays with his food or is continually diverted to something else Sexual desire is at first heightened but potency less

The symptoms vary widely in degree Mild hypomania may be an enviable time of well directed expansive energy unencumbered by some habitual restraints gross mania may be a delirious hallucinatory condition with incoherent talk and little free activity

SYMPTOMS OF DEPRESSION —In the early stages or milder forms the patient finds concentration and recollection difficult he has less interest and pleasure in life he feels that this world is unreal and himself changed he dreads effort or responsibility

The *mood* is one of grief and misery looking in every direction for material to feed on The past supplies peccadilloes or graver lapses what is wretched in the present is dwelt on inordinately the future is foreseen as hopeless ruin Anxiety is mixed with it often in extreme degree Weeping is less common in the extreme forms The patient s expression usually conforms to his affect.

Thinking is more difficult This retardation in thinking shows itself as incapacity to deal quickly and purposively with impersonal topics while brooding on personal matters goes on with a press of inner activity a ceaseless roundabout of painful thought The making of decisions is dodged Conversation may become meagre even monosyllabic though some patients are ever ready to tell their troubles The content of their thought is sombre—the product of ruthlessly unfair examination of their frailties and misfortunes Some criticise themselves remorsefully or with cynical detachment some bewail their losses others abandon themselves to resigned and world shunning despair There are many varieties of misery and melancholia knows them all—as many varieties as can be made from the experiences character and imagination of a human being Consequently they reflect the moral economic or hygienic standards of what is good and bad that are imposed on us by modern society and our particular education

Delusions occur in proportion to the depth of affect they are the extreme form of the doubts or preoccupations just mentioned Patients often fluctuate between uncertainty and conviction about their troubles even during the same day or the same conversation Insight may be good and judgement sound when the affect is not overwhelming The delusions are the product of the depression which is primary they are not its occasion though often adduced as that Most of them concern the future as well as the past anxiety is prominent Wickedness to be visited with damnation secular crime to be punished in this world loss of property that will

mean starvation and beggary for one's family mortal or corrupting diseases—these are the common substance of delusions and are often commingled For example some patients blame themselves for having caught venereal disease which will expose them to the loss of their job and of their hope of salvation exclude them from decent society and do loathsome damage to their bodies no evidence, no argument shakes the erroneous belief The delusions may be grandiose in that the patient affirms himself the chief of sinners no one has ever been as wretched or wicked as he he alone has done the unpardonable sin, or they may be of a minimising sort—nobody cares about him, he is of no account, let him go into a corner to hide people despise him This last belief is often understandably associated with ideas of reference or persecution—people make contemptuous gestures or remarks as he passes they set detectives to watch him they tell each other how bad he is He accepts this almost always as his desert though occasionally there may be overt resentment Apart from this resentment his beliefs derive understandably from his affective state There are however, features that betoken undercurrents at variance with the professed attitude or delusions Thus many depressed patients professing humility are importunate in their demands on those around them

Such hallucinations as occur are in keeping with the patient's affect and are of much the same nature as the delusions though expressed more in perceptual terms People are making derisive remarks his body gives off foul smells food has a different and disagreeable taste—it is often the mode of expression rather than of subjective experience that decides whether these are hallucinations or delusions This is notably the case with bodily preoccupations when for example patients report their food to be stagnating in their belly, their skin dull or fetid their eyes impaired their head empty Much of this depends on depersonalisation in which the body as a whole feels bereft of life and feeling and emotional deprivation or emptiness is translated into bodily experience In mild forms of depression there is no question of delusion or hallucination, and often no recognisable content to the gloom the patient cannot say why he is sad In the more chronic forms a settled and partly justified conviction about ill health, present troubles and the dark future prevails the ideas may be obsessional and partly divorced from the prevailing affect

Activity is limited thus contributing to the retardation' The more severe the depression the less does the patient do unless the concomitant anxiety makes him restless It is possible however, for a patient to be depressed without retardation In typical cases facial expression is rather fixed and movements delayed as though done against resistance more or less complex activities dressing say or writing a letter take unduly long The most extreme form is stupor or lack of all spontaneous activity it is seldom absolute Patients rarely become wholly indifferent to cleanliness in defæcation and micturition

Suicide is the greatest danger in depression Whereas manic patients thoughtlessly do themselves harm or get into a fight but do not try to get hurt depressive patients are often bent upon doing away with themselves The risk is not proportionate to the degree of depression many very retarded and melancholy patients make no attempt while in depersonalised mild cases a fatal outcome is not uncommonly brought about thus There is consequently much risk during the phase of improvement—often more risk then than during the preceding severe retardation Deliberate self mutilation is rare

Sleep is bad—hard to come by light and unrefreshing The *appetite* is bad too food may be constantly refused for this reason Commonly also the patient eats too little because of feelings of fullness and other discomfort in the abdomen or because of delusions about his bowels or his food Mild constipation is common but is often given much exaggerated importance by the patient *The weight* diminishes chiefly but not wholly because of insufficient intake of food Daily fluctuation in the general condition with improvement towards evening is common The skin

may be drv and sallow and in some severe cases pigmented as it is in pellagra Menstruation may lessen or cease sexual desire is much less There may be autonomic disturbance generalised or limited to a single system

Here too there are wide variations, between the mild neurasthenic and the grossly deluded melancholic who craves death There is every gradation between the two extremes and a single patient may during the course of the illness exhibit them all

SYMPTOMS OF ANXIETY —The *mood* ranges from uneasiness to panic stricken terror It may be an abiding or a recurrent state Though chiefly turned to the future as fear must always be it rests on past experience often painful and largely repressed and it reverts to the past to account for the troubles in store Herein as with rationali ation and some other psychological devices there is evident a strong desire to make things understandable in a causal nexus—a tendency to be found not only in patients but also in those who observe them The patient s expression varies with the strength of his fear

Thinking is troubled the disorder showing itself in speech somewhere between frightened dumbness and the voluble talk that seems designed to cover up embarrass ment and disquiet The patient can seldom follow a train of thought for long without a limited number of preoccupations forcing themselves in How far this interferes with daily life or set tasks depends on the amount of anxiety, as does also the impair ment of judgement and insight The content of thoughts is as manifold as in depres sion every normal matter of human concern enters into it. Fears centring strictly on a few special topics *e g* the fear of being run over in the street may be to the fore the fear of insanity is particularly common

Delusions are frequent in the grosser forms which are most strikingly though not exclusively seen in patients of late middle life They may say that their bowels are stopped up and their bodies about to rot their enemies are waiting to tear them to pieces their families will be tortured their names abhorred for ever Hell they are certain awaits their souls though their bodies cannot die time stands still and no redemption is possible There are many delusions less extreme than these mainly hypochondriacal and nihilistic ones *e g* beliefs that employment will be unobtainable or that the patient will be victimised for having had such an illness Hallucinations can occur at the height of fear every sound and sight and smell may be misinterpreted as meaning some pain to come but most of this is illusional colouring of actual percepts Depersonalisation is common with all degrees of anxiety

Activity is much disturbed There may be sudden attacks of panic in which the patient rushes blindly out into the open or aimless wandering ceaseless agitation with movements especially at the small joints—wringing of the hands rubbing the face picking at sores pulling out hair Starting many tasks and finishing none is as characteristic of anxiety as of mania Anxious people are distractable their eyes follow a trivial movement—a fly walking on the window pane—though they only comment on it when some interpretation that chimes with their mood can be fitted their ears are sharp for hints of alarm During an attack of anxiety with strong somatic repercussions activity may be completely interrupted—so called collapse—while the patient terror stricken expects his death alternatively he may run for air or help Very agitated patients may lie or sit in semi stupor with starting eyes and parted lips incapable of speech unless under some strong stimulus

Suicide is uncommon in those with episodic highly somatic attacks of fear and in those with chronic mild hypochondriacal anxiety but not infrequent in the grosser forms and in those mingled with depression

Sleep is bad in the mild forms the patient may be afraid to fall asleep because of his horrifying dreams and the terror into which he suddenly awakes

Sudden highly somatic episodes of anxiety are common the patient feels his

mean starvation and beggary for one s family, mortal or corrupting diseases—these are the common substance of delusions and are often commingled For example, some patients blame themselves for having caught venereal disease which will expose them to the loss of their job and of their hope of salvation exclude them from decent society and do loathsome damage to their bodies no evidence no argument shakes the erroneous belief The delusions may be grandiose in that the patient affirms himself the chief of sinners no one has ever been as wretched or wicked as he he alone has done the unpardonable sin or they may be of a minimising sort—nobody cares about him he is of no account let him go into a corner to hide people despise him This last belief is often understandably associated with ideas of reference or persecution—people make contemptuous gestures or remarks as he passes, they set detectives to watch him they tell each other how bad he is He accepts this almost always as his desert though occasionally there may be overt resentment Apart from this resentment his beliefs derive understandably from his affective state There are however features that betoken undercurrents at variance with the professed attitude or delusions Thus many depressed patients professing humility are importunate in their demands on those around them

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From obsessional disorder the diagnosis may be difficult when there is localised anxiety or depression with sharp content and good insight, so closely alike are the conditions that some authorities have proposed to include obsessional disorder also in the manic depressive group thus disposing of the diagnostic problem It is best however to keep them distinct and to discover in a particular case whether the characteristic subjective rejection of the obsession occurred at its first appearance often the anxious or depressive patient at the beginning has accepted the thought which accords with his affect though later he struggles against it and may disclaim it Genuine obsessions however are common in affective psychoses

Course and Prognosis—The varieties of outcome and sequence are many They depend on the balance between particular intrinsic and extrinsic causal factors in each case and on the extrinsic factors which are brought to bear on it in the form of treatment The more typical the illness the surer the recovery in favourable circumstances

A history of definite affective psychosis in a parent or grandparent points to recovery from the attack but it is unsafe to infer the course of the illness from hereditary data alone A well adapted personality and a pyknic build a history of similar illness followed by complete recovery a fairly sharp and fairly recent onset and precipitation by external troubles which will not be likely to continue are all of them points to the good Advancing years make the prognosis poorer but a first attack of melancholia in late middle life if there be no vascular disease eventually clears up in two thirds of the cases convulsant treatment has further improved the prognosis for this group Bodily changes are often the best indication of coming recovery Improved appetite and regularity of the bowels cessation of anxiety symptoms, clearing of the complexion increase of weight and return of menstruation may be noted, even before any increase of activity and long before any admission of feeling better can be got from the patient

A first attack of excitement or anxiety will seldom be the only one of depression it may Periodic depression and anxiety is less likely to cease in middle life than periodic excitement The occurrence of hallucinations or delusions is in itself of little consequence prognostically A transition from anxiety to depression or mania and from mania to depression or vice versa is commonly gradual Only in predominantly reactive attacks can one surmise *how long the illness will last* or when another attack is to be feared After recovery complete insight into what happened during the illness may not be attained especially by resentful manic patients melancholics who are sensitive and suspicious and agitated patients who feared personal harm

Generalised somatic disturbances *e g* loss of weight especially if acute and brief are of good prognostic import other things being equal The more the somatic preoccupations or symptoms are diffused over a period of time and localised to one system the poorer the prognosis this however does not apply so much to children as to adults Hypochondria and depersonalisation suggest a long illness as do nihilistic delusions (*e g* denying that one s bowels are opened at all) and to a far less extent admixture of hysterical or schizophrenic features The more the psychogenic causes have been obviously operative for a long period the greater the tendency to chronicity In the more chronic forms or after a series of attacks there may be impaired initiative and judgement irresoluteness dullness and social deterioration—none of them conspicuous Puerperal and pregnancy psychoses have a good outlook The milder forms of anxiety and depression if not already chronic respond well to treatment especially to psychotherapy

Death may occur from suicide insufficient food and intercurrent disease especially pneumonia

Treatment—PROPHYLACTIC—Genetic prophylaxis is occasionally possible as when two persons with definite affective disorders marry each other and are advised

heart palpitating his bowels turning over within him he sweats his limbs tremble his mouth is dry, he feels he will fall or collapse or die, he turns pale his pulse rate changes usually becoming more rapid, his blood pressure rises he may want to open his bowels or pass his urine When anxiety is long standing and severe such attacks are rare It is possible for parts of this general affective disturbance to be isolated and to occur with little conscious anxiety, as in muco membranous colitis effort syndrome aerophagy neurotic indigestion enuresis, impotence ejaculatio præcox psychogenic asthma hyperidrosis The factors determining such special emphasis on one or other system are partly physical (some organic defect or innate functional anomaly) and partly psychological In anxiety thyroid enlargement can occur, weight falls off menstruation is irregular or ceases, the deep reflexes are very active

Diagnosis —*Typical* cases are easy to recognise The common errors of diag nosis lie in (1) Missing organic disease (*e g* general paralysis, cerebral arterio sclerosis), or the converse (*e g* mistaking the more expansive manic patient for a general paralytic) (2) Forgetting how mixed the symptoms of mania melancholia and anxiety may be so giving rise to atypical pictures that may be mistaken for schizophrenia if too superficial an examination or too static and rigid a diagnostic criterion be used (3) Forgetting the influences of age general personality and milieu on the content of a patient s mind *e g* his having lived among spiritualists may lead to deceptively fantastic statements (4) Expecting to be able to diagnose solely on *presenting symptoms*, without regard to previous history and constitution the reverse is also to be avoided (5) Expecting diagnosis always to lie between distinct entities which could not possibly be mixed together in the same person, as though hysteria were incompatible with affective psychosis or both of these with schizo phrenia in fact, they often are mingled This is not to make light of diagnosis which gives the psychiatrist much knowledge that he cannot gain from study of the individual case before him

Nothing in the mental state of a patient with affective disorder may enable one to exclude an organic basis such as general paralysis or cerebral arterio sclerosis *This decision must turn on the physical findings* The problem becomes simpler when signs of dementia supervene (see p 1626)

From schizophrenia diagnosis depends on a picture of the whole illness, on the presence of characteristic thought disorder incongruity of affect and bizarreness of behaviour as well as on the previous personality and constitution rather than on any positive features of affective psychosis the remoteness and unconvincing manner of the schizophrenic so hard to describe but almost conclusive when recognised may help Later when complaints have become empty and repetitive to the point of stereotypy and catatonic symptoms mix with the anxiety diagnosis is easier As between schizophrenic and manic excitement the setting in which the excitement occurs is almost more important than the *prima facie* symptoms In young people schizophrenic features may often be found without their being of much significance, in the elderly what seem to be catatonic features may rest on an organic cerebral basis The more easily one can get in touch with the patient enter into his mood and under stand what he says and does the more is it an affective not a schizophrenic disorder The range of benign affective phenomena is wider than a textbook description can convey

There is no need except for administrative purposes to try to diagnose affective psychosis from psychogenic depression cyclothymia anxiety neurosis neurasthenia or involutional melancholia these are only subdivisions of it in which the age of onset reactivity severity or chronicity of the condition is being stressed Periodic recurrence is sometimes made the hallmark of affective psychosis this historically interesting point of view is hard to apply because so many patients have only one definite attack in their lifetime and because periodicity can be striking in other conditions such as obsessional disorder and schizophrenia

other hand some of them soon relapse For manic patients it is on the whole disappointing

Convulsant treatment by the electrical method has superseded chemically induced convulsions It is important that the psychiatrist should not use subconvulsant doses if he can help it The number of fits required varies from patient to patient but it is unwise ever to give a total of more than twenty fits Patients with circulatory or pulmonary disease should only be allowed to have convulsions after the risks have been fully weighed In order to lessen the chance of spinal or other fracture a relaxant is administered usually in conjunction with barbiturate intravenously

For the depressions of middle life convulsant therapy has enough success to justify calling it a specific method of treatment By the electrical method fits lasting less than a minute are induced three times a week not more than ten fits are usually required A relapse may necessitate repetition of the treatment Fragile bones or vertebral deformity may preclude use of the method unless special precautions are taken and the dangers made known to the patient or his responsible relative The treatment should not except in very special circumstances be given as an outpatient procedure It is capable of causing temporary and perhaps permanent cerebral damage though as a rule the forgetfulness or disturbance of consciousness which may follow the fits soon clears up In spite of the simplicity of the actual procedure —hardly more complicated than turning on the wireless—the tiro can do great harm with it by selecting patients who are unsuitable on either mental or physical grounds by giving too many or too few fits and by neglecting methods of preventing fracture and other complications

Patients with severe and long standing agitated depres ion sometimes are much improved by frontal leucotomy the longer they have been ill the less good is the operation likely to do

Prolonged baths—for 8 or 10 hours daily at a constant temperature of 96 to 98 F—have much value in allaying restlessness whether of the manic or the anxious kind especially the former They have the further merit of diminishing angry con tact with other people permitting fairly free movement and lessening dirtiness besides promoting sleep

Drugs are indispensable The fear of habit formation should not prevent hyp notics being given when there is persistent insomnia Barbiturates or paraldehyde often suffice it is well to ring the changes and to diminish the dose without the patient s knowledge For severe anxiety opium (*e g* as papaveretum) and hyoscine may be helpful the risks are obvious Continuous narcosis is valuable but must be used with caution Food must be given in adequate quantity and kind The induction of mild hypoglycæmia by insulin each morning may be helpful in inducing a willingness to take more food Artificial feeding preferably by nasal tube may be necessary because otherwise the patient would die of starvation The presence of acetone in the urine and a falling weight curve are strong indications that nutrition must be attended to promptly A good nurse may sometimes by unusual patience and sense get over an obstinate refusal to take enough food and drink but often nothing prevails against it Apart from hydrotherapy rest in bed fresh air atten tion to the bowels and other measures of general hygiene are desirable

Suicide is of the first importance Prevention of it can be better ensured by close knowledge of the patient and his day to day condition than by mechanical precautions but if he is bent upon it these may be unavoidable It is possible to make them unobtrusive without nullifying them Certain it is that excessive use of bolts and bars can defeat its own ends and excessive supervision aggravate a patient s misery his fears or his resentment Two good rules are (1) to discredit the maxim that those who talk of suicide never commit it and (2) to remember that most suicides are surprises Convalescence from melancholia is a risky time

Occupational therapy is good as soon as the patient can be got to co operate

not to have any children Rules of thumb do not apply in this matter it is wrong to tell a patient he should *marry or not marry*, procreate or not unless one has been able to weigh the dubieties of our genetic knowledge the pedigree of the patient and all his transmissible qualities with an informed and cautious judgement

Individual prophylaxis is not usually practicable until after symptoms have appeared which bring the patient to the doctor social prophylaxis and child guidance may, however have value in staving off or mitigating affective illness especially in those who are temperamentally very responsive to adverse circumstances *e g* in their domestic life their upbringing or their employment No satisfactory evidence is forthcoming that such measures *can forestall the grosser affective disturbances* necessitating mental hospital care which occur in highly predisposed persons In so far as one finds that environmental factors (*e g* heavy responsibility unemployment or sexual frustrations) have been important in provoking an attack advice on these matters may be helpful, it may be practicable by psychological and social treatment during the healthy interval to do much good in this way But some cases in which intrinsic factors seem all powerful, are proof against such measures and in any case it is not easy to persuade the patient when he is well again to put himself for a long time in the doctor s hands

TREATMENT OF THE ACTUAL ILLNESS —It is convenient to consider separately the acute major forms and the minor more chronic cases

For the former *the treatment other than by convulsions is directed to safeguarding* life relieving distress and providing the best conditions for the emotional disturbance to subside the situation is like that in tuberculosis or typhoid fever Exhortations to pull yourself together are as out of place as advice to take a voyage or an argument about the delusions If the attack is sufficiently severe to unfit the patient for ordinary duties treatment at home is probably inadvisable Although in such attacks all argument is futile and active psychotherapy harmful yet the loss of relation between current experience and emotion is never absolute there is virtue in separating the patient from real trouble and distressing associations reassuring him giving him firm kind management The essential combination of these and especially the last is rarely obtainable at home The patients however boisterous or suicidal usually *recognise their need of treatment and are willing to enter hospital* voluntarily They should not transact any business if it can be helped their judgement may be too much disturbed they lay up trouble for themselves Continuous narcosis sometimes curtails an attack it demands experience and care

Convulsant treatment is valuable most of all for involutional conditions least for mania Among involutional patients those with baseless suspicion and resentment respond less well than the self reproachful and agitated *It is still uncertain how* much benefit can be obtained in younger patients with acute affective disorder many of the figures purporting to show that in manic depressives (thus distinguished from involutional melancholics) the recovery rate after convulsant treatment is also high have been compiled from a series of patients the majority of whom had reached later middle life and might therefore have been properly classified as involutional It is moreover difficult to evaluate recovery rates for this purpose in a condition in which recovery is often obtained by other therapeutic methods such as would probably have been employed along with the convulsant treatment Whereas in the depressive conditions of late middle life there can be little doubt about the general superiority of convulsant treatment to any other available method in the affective *disorders of earlier life it is only by the effect* on the duration of the attack and the subsequent frequency and severity of attacks that the efficacy of convulsions can be judged the restricted information available does not give any conclusive general answer though it is evident that on the one hand some young patients have their attacks of depression promptly cut short by this method of treatment whereas previous attacks not treated thus had lasted for many months and on the

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but it is not rational treatment to pester a melancholic to encourage the fretful restlessness of the agitated, or to give the manic patient more things to muddle himself with and destroy Still it is often surprising to find how soon under tactful guidance these patients will enter into ordered activity of a more or less simple sort, and how helpful it can be to them During the stage of improvement the same is true of recreations and social activities Patients should not leave hospital till recovery is assured unless it is obvious that the hospital surroundings and the absence from home and work are an actual cause of their persistent anxiety or dejection

To revert to the *milder forms which tend more to become chronic* Here manipulation of the conditions in which the patient lives at home and at work may be conjoined with psychological treatment (individually or in a group) depending on an appraisal of the causes of his illness There is nothing distinctive (though much that takes account of the individual patient s needs) in the psychotherapy and social treatment called for (see pp 1618 1619) danger signals must be recognised as they occur Zeal must give way to the real needs and resources of the patient which are often not appropriate to a drastic or very lengthy treatment Simple measures of enquiry explanation and reassurance, together with small environmental changes may have much effect A fixed régime imposed in detail by the doctor is helpful, this becomes more and more necessary as the affect dwindles in long standing cases Hypomania does not usually respond to causal treatment of any kind it seems to run a largely autonomous course Anxiety may yield very satisfactorily to patient psychotherapy and environmental adjustment

SCHIZOPHRENIA

Definition —The forms of illness under this name are so diverse that many efforts have been made to distribute them so far in vain What is common to them all is a detachment from the world without and a breaking up of normal psychological connections within The personality is not integrated as in normal people thinking emotion and conduct are discrepant and morbid yet there is no impairment *of formal intelligence such as is found* for example, in organic dementia The obsolescent name dementia præcox is not a synonym for schizophrenia but a reminder of its recent history At the end of the last century a large number of patients in mental hospitals were found to have begun their illness before they were 30 and to have passed ultimately into a deteriorated state that looked like dementia their illness was closely studied delimited and called *dementia præcox* When the same clinical picture however came to be found in cases that had not such an outcome or onset, the latter criteria were waived in favour of a descriptive analysis of the actual symptoms and along with this larger conception came the new word schizophrenia which betokened a more psychological approach and a more elastic and generous notion of what might be included Theories of *causation* psychopathology and clinical boundaries are implicit in any view of what schizophrenia' really is consequently it is still possible for two experts to disagree about what should properly be included under this name yet over the diagnosis and prognosis of any particular patient they will attain a measure of agreement and certainty surprising to those who know the condition only from reading or limited experience

Ætiology —INTRINSIC —The intrinsic factors are very important Studies of the incidence in twins and in the members of a family demonstrate a hereditary factor in a majority of cases If one of a monozygotic pair of twins be schizophrenic *the other is also in 76 per cent* of cases whereas the corresponding percentage among dizygotic twins is only 14 The nature of the mode of transmission is still in doubt the most recent observations suggest a single recessive factor which must be inherited from both parents Variations in the manifestation of the disorder may be in part

dependent on a non specific character controlled by a multi factorial genetic mechanism

The constitutional features that betoken an innate predisposition to this illness are more of the psychological than the physical kind The bodily attributes have been said to be an 'asthenic or ectomorph' (weedy and lank) athletic or dysplastic build but since these are found in much the same proportion among healthy people as among schizophrenics and the correlations between habitus and diagnosis are not convincing there is little to be said for them here It is however certain that pyknic build (see p 1646) is uncommon among schizophrenics More significant however are the features of personality commonly called schizoid they are to be found in a large number of cases though not by any means in all The patient is reported to have shown slight peculiarities from his earliest years he has been quiet shy and solitary a ' model child , given more to daydreaming or abstract speculation than to ordinary interests and activity sometimes he has been unduly submissive and sentimentally affectionate or touchy suspicious obstinate and resentful of advice and control A single typical schizoid personality is a *myth* It is moreover to be stressed that a frozen description of the schizoid varieties of personality does not do justice to the true state of affairs characteristic deviations from the conventional norm of behaviour can always be understood better if the patient s way of dealing with his circumstances is viewed historically as a biography of individual tendencies and experiences rather than described as a bundle of traits By paying heed to the development of faulty as well as healthy habits of response the psychiatrist can often see the march of events that led up to the patient s illness and escape too artificial a sundering of inherent tendencies from the external happenings by which these tendencies have been evoked and given shape and substance

EXTRINSIC —The illness sometimes breaks out after childbirth or an acute infection None of the efforts made to inculpate some specific infection have succeeded nor has intoxication in general been found to play any considerable part in the causa tion of schizophrenia The same is true of cerebral trauma There are however many instances of a chronic schizophrenia supervening on an intoxication and of schizophrenic symptoms especially of the catatonic sort appearing in the course of an organic disorder such as G P I or encephalitis lethargica In these the same structural and functional systems must be supposed to have suffered impairment as in the endogenous forms of schizophrenia and it has been particularly urged that in the chronic paranoid conditions that may follow an acute alcoholic psychosis it is really a matter of schizophrenia that happens to be associated with alcoholism if not partly activated or released by it It is further to be remembered that certain intoxications *i e* with mescalin lysergic acid or adrenochrome produce a mental disturbance that is in some respects similar to schizophrenia, and that any chronic *hallucinosis comes in time to look very like a long established schizophrenia probably* because the possibilities for abnormality of any human mind are few the deprivation symptoms almost uniform and our methods of clinical examination imperfect Endo crine disorders especially of the gonads have been held responsible but are more probably manifestations of emotional disturbance findings are not consistent and the relation between endocrine and psychological events still rather obscure

Recent mental stress may sometimes be the starting point of an attack but in a considerable proportion of these cases the reported overwork disappointment in love or other painful experience, is found to have been a product of the already existing illness or the last of a long series of disturbing events No recent experience is ever sufficient to account for the illness without regard to intrinsic causes Nor is any remote experience either No matter how searchingly the patient s life be resurrected and analysed it is scarcely ever possible to discover that anything happened to him which would have led to his adopting a schizophrenic way of shunning daily life unless he had been somehow disposed to it from the beginning although of

course much may have happened to him that has strengthened and fostered the disposition

Among contributory factors, age and sex are noteworthy An onset after the age of 40 is uncommon In three quarters of the cases that later exhibit the characteristic chronic syndrome the illness begins between 15 and 25 *The condition may* become overt in children before puberty Men are more often affected than women—in the proportion of 113 to 100 according to the largest available statistic the matter is dubious however, because of the different standards of diagnosis used

Pathology—PHYSICAL—Histological changes in the brain are not characteristic it is doubtful if they are even frequent A cellular loss in the third and fifth layers of the cortex with lipoid accumulation has been found but *it occurs in many* other conditions Swelling of the oligodendroglia has been described in brain tissue obtained at biopsy Many claims about cerebral pathology and the chemical and physiological changes in schizophrenia have now been discredited *so that all findings* in this difficult field have come to be matters of suspicion Variations in the same individual may be wide Investigations have purported to show a disturbance of the acid base equilibrium towards the acid side with a diminished excitability of the respiratory centre to carbon dioxide lowered rate of oxygen consumption polyuria diminished gastro intestinal motility poor response to epinephrine, insulin and dinitrophenol, and to vestibular stimulation by cold water or rotation abnormal heat regulation, abnormally variable sugar creatine and non protein nitrogen content of the blood anomalous capillaries decrease or sluggishness of total blood volume, and slowing of the arm to carotid circulation time These findings indicative of a defect in adaptive capacity have not so far been controverted they represent disorders of metabolism and regulation which may be partly a concomitant of the characteristic mental disorder and partly an effect of it *i e* they may be essential physical disturbances in the illness, or may be secondary to the abnormal often inert life the patients have led since they became ill thus evidence of hepatic dysfunction in catatonic patients is of nutritional origin and may be corrected by changing to a suitable diet

Some inferences have been drawn from the similarity of catatonia to the extra pyramidal syndrome that can be produced in animals by bulbocapnine the argument from analogy cannot be pushed further than to say that certain functional systems are available in the brain disorders of which are sometimes evident in schizophrenia as they also may be in poisoning or in encephalitis lethargica G P I and other diseases

Very significant are the well attested metabolic findings in the rather rare cases of cyclical catatonia In these the nitrogen balance varies periodically with alternating phases of retention and over excretion corresponding to the mental change from excitement to stupor or vice versa By means of thyroxine a thorough *emptying* of the patient s nitrogen store can be brought about and subsequent nitrogen retention prevented thus leading to clinical improvement The correlation between metabolic happenings and clinical condition in these patients is *now established*

PSYCHOLOGICAL—The large and inconclusive literature on the psychopathology of schizophrenia derives from

(1) Minute description of the phenomena observed and abstraction from them of general principles of disordered function
(2) Experimental study using projective sorting reasoning and other tests as far as possible under controlled conditions
(3) Studies of artificial hallucinoses (*e g* mescalin intoxication) and parallel experiences
(4) Comparative study of animals *children poets primitive* people etc.
(5) Intuitive or speculative interpretation

It will be obvious that these methods overlap and that they differ widely in

acceptability and usefulness The findings of almost all can sound plausible when stated in general terms discrepant or abstruse when stated in detail Their exposition touches on the most intricate problems of normal and morbid psychology and therefore is highly technical and unsuitable here A working hypothesis for clinical purposes is that in schizophrenia there are inherent faulty dispositions whose manifestation depends in severity and persistence on upbringing and other external circumstances It is characterised by among other things a perversion and failure of synthesis so that there is an inco ordination intrapsychic ataxia as it were a splitting up of the mental life which justifies the name Schizophrenia The whole psychic life of the patient cognitive emotional and conative may be changed in a way that is alien to normal understanding We can observe the change but to enter into it or describe it adequately in terms of our own experience is far more difficult than if we try to do this for depression manic excitement hysteria or obsessions It shows itself also as a turning away from the contacts and realities of daily life a preference for what the mind can supply from its own stores however morbidly rather than for the current experience that the outer world affords

Symptoms —Schizophrenia may be regarded for clinical purposes as a form of maladaptation in which there are characteristic defects of inner harmony and consistency in behaviour thought and emotion These are rarely seen in childhood but from puberty onwards they may appear in varied combinations (often in persons who for years have been introspective and unsociable) There is discrepancy between mood and utterance disturbance of conduct (briefly summed up as catatonic or hebephrenic) self absorption and incapacity for sustained thinking along normal lines A guarded or artificial demeanour may conceal these essential features whereas they may be conspicuous in a florid or deteriorated case Hallucinations and delusions may fill out the picture affective or other morbid types of reaction may complicate it

The onset is not always abrupt There is often a long history of preliminary symptoms in which it is arbitrary to decide where personality has merged into illness Complaints of headache weakness anxiety attacks loss of appetite and dysmenorrhœa may have accompanied slight oddities of behaviour such as rudeness or apparent absence of mind and indecision The patient may have felt an alarming change in himself in his capacity to think and feel normally and been notably depressed and anxious Ideas of persecution or of exaltation may occasionally escape him or he may have become stilted in his talk and shown other affectations and mannerisms The more gradual the onset—and in many cases it has spread over many years—the more unlikely is it that it will have been recognised as morbid

The commonest or basic symptoms are (1) Disorder of thinking (2) Emotional incongruity (3) Hallucinations (4) Disturbed impulses or conduct From these can be derived most of the other symptoms such as delusions feelings of influence autism catatonic phenomena anomalies of speech negativism and the rest

The *disorder of thinking* is a characteristic and central feature The patient cannot command the whole range of an act of consecutive thought he misses the point fastens on details and brings in irrelevant associations which are correct in themselves but which divert him from the main end of his original process of thought consequently his thinking is incoherent rambling and jumbled He brings together the most far fetched topics so that the connections are sometimes so superficial as to be empty of meaning and at another time profoundly influenced by symbolism and highly individual values The usual logical sequences are ignored cause and effect are interchanged temporal spatial verbal and accidental relationships are unduly turned from abstract to concrete treated as grounds of identity played with or flouted Things linked only by analogy and chance association are taken to be the same The condensation of several conceptions in one or transference of a set of attributes to some inappropriate object may become a matter of course so that only the closest knowledge of the patient and his surroundings will enable the psychiatrist

to follow his meaning It is not necessary however that such extreme *incoherence* be evident in the patient s talk he may not show any at all when speaking or may suddenly obtrude a startling lapse from normal ways of thought which he then ignores justifies or explains away Inconsistent thoughts can be present together in a way impossible for normal people and the same object or notion can appear to him in several interchangeable guises each of which would normally exclude the others The patient himself is often aware of his disordered thinking and may describe it he feels his thoughts are suddenly taken out of his mind other thoughts foreign to him are put into his head, his mind is not his own his thinking is suddenly interrupted, some external power controls it

The thought disorder is illustrated by the following characteristic remarks of patients There were bats and bees coming through the window, of course that was because my brother in law kept teasing me He said I had bees in my bonnet' 'If I should return during my absence, keep me here until I come back' I have a lot of forced thoughts My thoughts are all drawn out words they ought to be pin pricks There is an unnatural stoppage in my thoughts, too I have heard voices say, He is conscious of his life To get my feeling back to normal I feel like changing motor cars into battleships to be superior to them

This disorder may only be demonstrable when the patient gets on the topic of his delusions in other matters he may seem quite sensible It is not essentially different from what normal people experience during states of altered consciousness *e g* in dreams or when falling asleep, the schizophrenic however has it with clear consciousness so that a listener often feels that the patient is making fun of him in giving such transparently absurd answers with an air of knowing exactly what he is about A chronic well preserved schizophrenic has been known to make his living as a comedian the audience much enjoying the allusive, half comprehended nonsense with its background of innuendo and symbolism Autism *i e* immersion in his own fantasies and preoccupations may account for much of the oddity and detachment the patient shows it accounts also in part for his negativism , in that he resents any stimulus that interferes with his daydreams

Delusions arise mainly out of the thought disorder They are often bizarre they may occur to the patient with a suddenness of conviction that puts them beyond all argument and they are egocentric in that they commonly bring indifferent happenings or people into a special relationship with the patient—*e g* he suddenly knows that when his cousin yesterday said he had been reading about Napoleon s divorce of Josephine it was a subtle way of telling the patient that his wife was committing adultery with this cousin whose name is Joseph The delusional ideas may not be firm conviction but fleeting notions readily given up and based upon some casual instance of the thought disorder, sometimes they are schizophrenic ways of saying something commonplace—*e g* the patient declares his wife has poisoned him but when he is further questioned says airily that he means she gives him ill cooked food which is bad for his digestion

Fixed delusions are however common and are usually of a paranoid complexion they may develop out of more or less ephemeral ideas of reference They are often intermixed with hallucinations The patient gets into a state of mind in which he feels there is meaning in everything something is going on behind the scenes he is perplexed by all this and mystified it has to do with him in some uncanny way Presently, he begins to see through it all sometimes he gives it some religious or cosmic significance, especially if he has much anxiety as well—the Last Judgement is at hand he is to be responsible for the regeneration of the whole world The delusions are not always enacted on so grand a stage there may be homely fancies about neighbours who whisper and sneer, or about some bogy like the Jesuits or the Jews or the C I D Often the patient complains that people work on his mind hypnotise him influence him for his own good set about to drive him mad or ruin

him Delusions of grandeur may be linked up with these paranoid ones (*e g* he is being persecuted because he is the Messiah) and may be likewise pedestrian or lofty according to the patient s previous education and interests the severity of his dis order the copiousness of his fancy and the amount of normal mental function still in evidence Here as elsewhere in psychiatry the symptoms are a mixed outcome of impaired or perverted function on the one hand, and of normal function on the other the latter either reacting to and modifying the disorder or obtaining freer play through it If for example a patient feels his thoughts being controlled by some external influence and he has queer tinglings in his body his conviction that he is being hypnotised and that someone is playing an electrical instrument on to him must be regarded as a normal attempt to find the cause of an almost inexplicable happening The delusions are sometimes about past events which are falsified retrospectively *e g* the patient relates details of his having been a changeling or a predestined hero Delusions about bodily transformation or disease are frequent, and may be complicated and bizarre

Patients often do not act in accordance with their delusional beliefs especially when these are fleeting or chronic they may for example be friendly towards a nurse whom they believe to be persecuting them cruelly But this is on the whole unusual in the early or acute stages of the illness a patient will then act on his beliefs violently or in terror he may go to the police or be driven to suicide

Constantly the matter of a patient s delusions will be found to be intimately dependent on his experiences his emotional attachments and sufferings his struggles and frustrations it is impossible however by any such analysis and derivation of his delusions to account for the fact of their occurrence *i e* for the patient s choice of this way of dealing with the experiences in question The same is true of the general thought disorder *e g* interruption or blocking of the train of thought may take place only when some emotionally weighted topic some complex is touched on This accounts for the place where blocking occurs but not for the blocking itself that like the other fundamental disturbances of function in schizophrenia eludes a wholly psychological explanation

Intellectual defect does not occur though the patient may find it difficult to form concepts necessary for abstract thinking There is usually no clouding of conscious ness Intellectual laziness or evasion is often conspicuous the patient may repeat questions in a musing way or profess ignorance Orientation and memory are not as a rule diffusely impaired though hallucinations delusions and lack of interest may interfere with them and consciousness may be disturbed in stupor or excite ment Many a patient who has long borne the appearance of gross dementia will suddenly show that his intelligence is still a sharp instrument drugs *e g* sodium amytal or insulin and intercurrent disease or shock can thus dramatically reveal how little ground there is for calling this illness a dementia Schizophrenics often do the unexpected Amnesias and deliria when they occur in schizophrenia may be hysterical obsessional and hysterical symptoms like anxiety and depression are compatible with schizophrenia and are often an intimate component of the illness

The speech and writing of the schizophrenic betray the extent of his thought disorder Stiffness pedantry fantastic euphuisms words of his own coining queer symbols and grammar stereotyped repetition and infantile twists like speaking of himself always in the third person may be conspicuous features of the patient s use of language There may of course on the other hand be little or nothing outwardly amiss in his conversation and writings In florid or chronic cases the patient may talk in an unnatural voice or without any modulation Writing may be set forth as though it were painting and the converse in subject and matter the patient s in sanity may be patent but his treatment of his matter however odd, is seldom odder than some forms of art and it cannot be called typical of the illness These anomalies of symbolical representation are as open to psychological explanation as are the

delusions mentioned above the neologisms for example can be analysed up to a point and these phenomena have enriched our knowledge of the psychopathology of schizophrenia

The *emotional incongruity* is the chief, but not the only, sign of disturbed affect Often the patient himself notices in the beginning of his illness that he is less moved by habitual affection or even feels hatred towards a parent he has loved The strongest and rarest of human passions are not infrequent in this illness ecstasy mystic communion despair, horror agony of death limitless abandon apotheosis salvation are approximate names for these exceptional states that are probably indescribable in the current language of normal people Apart from these and much the commonest of the affective changes is apparent emotional shallowness the patient receives moving news without any sign of being touched by it or his response is perfunctory he smiles or looks bored when talking of a recent tragedy in his own family This shallowness and incongruity of affect is however not to be taken at face value What the patient says and what he means with his words, may be very different so may what we say be very different from the meaning the patient attaches to it *It is unsafe to assume that the patient s words have reference to what is mainly* going on in his mind at the moment or that his outward expression is a trustworthy index of his emotional state Violent emotional outbursts—of anxiety rage love misery—can certainly occur in a patient who has lately seemed empty of all affect The schizophrenic patient is undoubtedly different from normal people in his emotions but not in so negative a way as his seeming apathy and lack of affective rapport would suggest His attitude towards the same person may change quickly in accordance *with conflicting or opposite tendencies in himself*, *this ambivalence is often* understandable in the light of his earlier history Sometimes the illness leads to a blunting of ordinary reserve a lack of reticence, or a levelling down of the gravest matters so that frivolous or cynical indifference and imperturbability are signs of the patient s morbid condition

Hallucinations are not so frequent as superficial examination of patients might suggest many of the patient s assertions about queer sights and sounds are not the *expression of vivid perceptions but of passing fantasies imagined more* plastically than is normal this is particularly true of many of the so called visual hallucinations or of cases where the unreal perceptions occur in several senses together Hallucinations are nevertheless extremely common and persistent in schizophrenia auditory ones occur most often diffuse somatic ones not infrequently those of smell taste and sight more rarely

The voices are sometimes so closely linked with the thought disorder that it is difficult to tell whether the patient is relating what he has heard or what he has thought He may show the intermediate stages between the two declaring that people repeat his thoughts or that everything that passes through his mind is spoken aloud inside his head his actions are described publicly he cannot go to the lavatory without shameless comments What the voices say may be abuse or encouragement trivial repetition or threats and commands this content can usually be accounted for by the psychiatrist when he knows the patient and his history well The voices may come from strange places *e g* from inside the patient s own chest or abdomen and are then often accompanied by curious somatic hallucinations indicative of morbid attitudes both physiogenic and psychogenic towards parts of the body The latter often occur independently Queer sexual feelings or distortions and impossible growth of *various organs may be reported* They are usually bound up as any schizophrenic symptom is likely to be with delusional and emotional components which are partly derived from the patient s experiences and psychological development The visual disturbance like the gustatory is more often illusional than hallucinatory *e g* people s faces *look fiendish or artificial or transfigured*

The *actions and bearing* of the patient are often characteristic. Abruptness or

lack of grace in movement may be seen early it can be indistinguishable from the fidgety self conscious hobbledehoy stage of adolescence The patient may pull faces at himself in the mirror or may be unaware of his grimaces Asymmetrical move ments of expression twitchings mannerisms queer rituals and tic like gestures are to be met with The meaning of the patient s movements can usually be worked out but after they have been present for long their sharpness is rubbed off, as it were and the empty stereotyped movement at last gives little clue to what was once a significant emblem of experience and feeling The movements often seem to become automatic, like the ' verbigeration of empty phrases in the patient s speech Nega tivism talking and acting beside the point and bizarre escapades may be seen at any stage of the illness

There may be a suspension of movement or the reverse akinesis or hyperkinesis Both may occur in the same patient who may lie for weeks or months in a catatonic stupor from which he suddenly emerges into swift action He may carry out some impulsive action and then promptly return to bed and stupor or he may become wildly excited and imperil his life by his blind and raving activity During catatonic stupor patients may adopt strange postures *e g* holding their head off the pillow all day pursing their lips They may be indifferent to cleanliness about fæces and urine or actively dirty in this regard Waxy flexibility is rare but many patients are auto matically obedient so that they keep up an imposed posture

The variety of schizophrenic anomalies of conduct is too great to be described here They must not be assessed absolutely but always in relation to the setting in which they occur Then they have meaning in the individual case and are not merely so many examples of ambivalence or mutism or negativism ' It is however true in this matter also that understanding the content of an anomaly does not make its occurrence likewise understandable Much of the schizophrenic s conduct is so close to certain disorders of movement in organic disease of the central nervous system and its connections that somatic mechanisms may be assumed to have suffered damage in this condition There are three main things to be done with any schizophrenic symptom (1) to search out its psychological origins and its meaning for the patient in his present situation (2) to link it up with the other functional disorders that he shows and (3) to consider its background of physical structure and function It is not always practicable to attempt all three nor is it as yet possible to do them well but none can be ignored without detriment to a full analysis

Often the most significant yet intangible effect of the illness is upon the patient s *personality* After florid symptoms have died away or when there are no definite symptoms at all a change in the patient s ways is remarked by his intimates Not only is he outwardly different—more peculiar less understandable and predict able rather shut in upon himself remote with queer values and impulses—but in many cases he is also aware of this change and may complain of an inner perversion of himself a loss of that unity which we take for granted when we say I or me Insight in schizophrenia in this respect and more generally too may be penetrating and just as many self descriptions attest There may also be varying degrees of impairment up to gross lack of insight

None of the *bodily symptoms* are characteristic of this illness though many occur Besides the somatic complaints and preoccupations already mentioned patients especially if young show vegetative anomalies Thus vasomotor disturbance may take the form of cold bluish extremities exanthems or œdema Seborrhœa is common Abnormal growth of hair occasionally occurs in women Loss of weight in the acute stages and fatness in the chronic condition interruption or irregularity of menstruation and fluctuations of temperature may also be observed especially in catatonic cases of the schizophrenic states stupor is the richest in demonstrable bodily changes Fleeting neurological signs *e g* pupillary anomalies may be found

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that the speech and acts of the latter are intelligible as expressing a general affect and are conformable to the situation in some measure the onset and cessation are not so abrupt as in catatonic excitement and there are usually characteristic features which make the distinction easy Melancholia becomes suspect when delusions are repeated without the appropriate effect, and there is a readiness to project responsibility for the illness to complain of external influence The inertia of the depressive is not so complete as that of catatonic stupor, nor so likely to be abruptly broken through States of severe agitation are not always easy to distinguish from schizophrenic excitement, but a more frequent problem is that of deciding whether some bodily fear or conviction of disease is schizophrenic or not Whether in regard to a preoccupation or a delusion the chief point to consider is the appropriateness of the affect to the alleged hypochondriacal notion, the more bizarre the bodily change described, the more likely to be schizophrenic Depersonalisation is sometimes at the bottom of these somatic complaints what is significant is not the depersonalisation but the way it is elaborated and regarded by the patient

Hysteria can offer great difficulties largely because hysterical mechanisms are so often operative in schizophrenia Plain motor or sensory disturbances commonly give less trouble than hysterical dissociation stupor and pseudo dementia The *previous history the relationship of the outburst to a particular set of happenings* the behaviour in the intervals the demands upon the attention or response of by-standers must be taken into account The mistakes and oddities of the hysterical pseudo dement may be theatrical in accordance with his ignorant notion of what insanity is like the deliriously dissociated hysteric does not identify correctly the people around him as the schizophrenic usually does even when in a dream like state the hysteric who is acting some imagined scene does so without discrepancies or gross interpolations whereas the schizophrenic is seldom so consecutive and persistent The degree to which the patient is being influenced by his immediate surroundings is however the chief guide apart from definite schizophrenic features

Obsessional states offer difficulty when the patient is in doubt as to whether his alien thought or impulse comes from within his own mind or is imposed upon him If he shows indifference as to the occurrence and content of the compulsive ideas it is suggestive of schizophrenia but careful examination of the development of the symptom and the patient s attitude towards it permits a clear diagnosis in most cases Complicated rituals odd obsessions and chronicity make an obsessional illness look very like schizophrenia as does intoxication of an obsessional patient by bromides Obsessions may develop into schizophrenic symptoms (see p 1679)

Prognosis —Schizophrenia is always a serious condition Though some recover the tendency of this morbid change is to do permanent damage to psychic life In the individual case however pessimism is not justified It is certainly never possible in the early stages of the illness to be certain that recovery is out of the question

Heredity is a poor guide to the prognosis except in the rare cases in which an identical twin of the patient has for some years had a schizophrenic illness or in which one parent is schizophrenic and the other has schizophrenic relatives even then it is difficult to prognosticate with assurance regarding the present attack If one parent has had an affective illness the prospects of recovery are brighter but this can better be assessed from the patient s own bodily and mental constitution If he is of pyknic build the outlook is much better Similarly the patient who has for years tended more and more to withdraw from his surroundings to be careless of social requirements to lie late and live alone given up to day dreaming and eccentricity—such a one should he become overtly schizophrenic has a poorer chance of doing well than the active suspicious and impulsive man or the self conscious introspective worrier who similarly falls ill A narrow and rigid previous personality makes deterioration more likely than if there had been wide interests and possibilities of adaptation

In states of acute excitement attacks of unconsciousness may occur but epileptic seizures are very rare

VARIETIES —*There are three main forms*—catatonic (with acute outbursts) hebephrenic and simple (early onset chronic course), paranoid (fairly late onset delusional) They are not exclusive categories and it is usually profitless to try and apportion a doubtful case to *one or the other* They do not correlate closely enough with outcome or effective form of treatment to be of much use clinically

In *hebephrenia*, the least common variety delusions and hallucinations are inconsiderable but *abnormal conduct is to the fore* the patient may be silly and mischievous abruptly eccentric or inert and without initiative The illness may progress without acute episodes (dementia simplex) or be interrupted by phases of excitement or *obvious insanity which subside, leaving* the patient worse than before In *catatonia*, the most favourable variety the symptoms are plain even to the layman akinetic or hyperkinetic states may appear and subside quickly, sometimes for good or *for several years There are usually*, also, characteristic disorders of thought and emotion which may clear up when the stupor or the excitement does In the *paranoid* form, generally rather late and insidious in its development but less damaging to the *personality than the hebephrenic, partial systematisation of the* delusions is common in the earlier stages but may be later swallowed up in the general thought disorder and deterioration (dementia paranoides ') The more bizarre the delusions the *more likely is affective emptiness to replace gradually the initial* resentment and distress but sometimes the patient passes into a chronic paranoid state obviously schizophrenic to the psychiatrist but compatible with ordinary life outside an hospital Hallucinations and luxuriant delusions may however be conspicuous in the paranoid form (paraphrenia and dementia phantastica)

Diagnosis —The chronic and advanced cases— typical dementia præcox — *that abound in mental hospitals are easy to diagnose but early or inconspicuous* cases often extremely difficult The chief positive points to look for are characteristic thought disorder a qualitative change of affect and other evidence of intrapsychic *ataxia as well as feelings of being under external influence* Catatonic symptoms are of limited diagnostic value because of their frequency in organic and symptomatic psychoses More important than any single feature is the impression of the cases as a whole the development away from normal interest and response to the real world and the establishment instead of autistic self satisfactions so that the patient s personality is twisted awry as it were and withdrawn from easy contacts

It is unsafe to lay much weight on the diagnostic help afforded by projective and other psychological tests The intuitive element in the interpretation of Rorschach and other findings of this kind is greater than is consistent with a reliable diagnostic procedure The psychological data may suggest schizophrenia but should not be the decisive factor

From organic syndromes—syphilis of the central nervous system alcoholic psychoses disease of the cerebral vessels encephalitis lethargica etc —*the differentiation* turns on the physical findings more than on the mental state a schizophrenic syndrome may appear in an organic condition because the brain as Kraepelin said is like an organ whose stops give out the same sound whoever works them Often it is not a matter of deciding whether the syndrome is organic or schizophrenic *but* whether being schizophrenic it has a discoverable somatic basis or not Alcoholic delusional states are an instance of the complicated relationship that may be found (see pp 1638 1639) If after consciousness has become clear *again the other* phenomena of toxic confusional psychosis persist then schizophrenia is the more probable diagnosis

Diagnosis of schizophrenia *from an affective syndrome is* difficult because both are often combined in the same patient. Some of the significant points have already been referred to (see p 1652) Catatonic excitement differs from mania in

into ordinary life as soon as possible provided conditions there are not too adverse for him or he too abnormal to cope with them

Treatment in a psychiatric clinic or mental hospital is usually necessary at some stage of the disorder and must be decided chiefly by the severity and social risks at the time For the large number who become permanently in need of institutional care much of the deterioration formerly customary may be averted by the energetic use of occupational therapy and recreation which make the patient s life less sterile The term total push has been applied to a programme having this object, and attaining its social end in proportion to its vigour in using all available means of stimulating and encouraging the individual patient

There are few conceivable ways of altering a human being that have not been tried in this illness Many of them have been those believed to be efficacious in other illnesses some have been intended to shock the patient somehow Of the former may be mentioned thyroid and other endocrine preparations (in large doses) transplantation of gonads removal of supposed septic foci induction of fever by malaria etc injection of human serum, manganese salts production of aseptic meningitis hypothermia and continuous narcosis Of the latter *i e* shock methods many of the procedures of a bygone time are examples the whirling chair, precipita tion from a height, immersion in ice cold water and so forth The most recent methods which entail a profound disturbance are those which use insulin or a con vulsant (see p 1621) The convulsant method has been of value in some acute stupors and conditions in which, along with the schizophrenia there is a considerable affective admixture

The value of insulin treatment is variously assessed some believe that it should be given to every schizophrenic as soon as his condition is recognised others that it benefits those who would get well with other forms of treatment if administered with equal zeal The former say that it shortens the duration of illness and increases the number of recoveries the latter insist that this improvement is seen to be largely spurious if a follow up enquiry is made into the later course of the patients lives That such extreme views can be held by responsible observers relying on large series of cases is due not only to their prejudice and temperament but to the difficulties of judging therapeutic success in an illness which is sometimes difficult to diagnose with certainty in its early stages is often accompanied by another more benign mental illness and has anything but a uniform prognosis moreover it was believed to be hopeless by many psychiatrists in pre insulin days so that they did not try to treat it by methods then available which would have yielded full permanent recovery in a quarter of the cases if selected on the same basis as is now customary for insulin treatment It was the general experience before the advent of insulin that a third of the schizophrenic patients who were admitted to an active psychiatric hospital within a year of the onset of their illness got better with general treatment and remained capable of life outside a hospital mass figures from a heterogeneous collection of psychiatric hospitals showed less satisfactory results This partly accounts for the discrepancy between those who report remarkable improvement in the pro portion of schizophrenics who recover now that insulin has been used for their treatment and others who cannot discover any statistically recognisable difference in efficacy between conservative treatment and the insulin method under comparable conditions of case selection and management An additional cause of discrepancy in results lies in the different methods of administering insulin treatment Some aim at giving the lowest dose of insulin that will produce coma others prefer the highest dose that can be given without endangering the patient s life some let the comas continue for 3 or 4 hours others terminate them earlier and there are even advocates of comas protracted up to 15 hours for patients unresponsive to milder measures, hypoglycæmic convulsions are regarded by some as therapeutically valuable by others as harmful Insulin and convulsant treatment have demonstrated beyond dispute

The more abrupt and stormy the onset, the better the outlook This is one of the most reliable guides When the onset has followed upon a recent painful experience and the content of the patient s talk and his behaviour refer to this or when a physical damage appears to have provoked the symptoms (*e g* influenza or head injury), the outlook is rather better than when the provoking factors are obscure but this is by no means always the case If the attack occurs during puberty or adolescence prognosis must be cautious because of the difficulty of distinguishing between the transient upsets of this period of adjustment and the progressive schizophrenia that may then show itself plainly The earlier history is of great help

The nature of the symptoms is not a safe guide Very severe departures from normality may clear up yet an outwardly mild condition be of grave omen Symptoms such as stereotypies of movement and speech which indicate that the illness has been going on a long time and that there is a general narrowing and fixity are grave as are also hebephrenia and a long drawn-out stupor with negativism impulsive violence and vasomotor changes The more manic or depressive features the better Previous attacks with an interval of normality between them, are prognostically favourable If the patient first falls ill after 30 he will scarcely go downhill in the tragic way young people sometimes do He may develop fixed delusions which are often rigid and encapsulated, so to speak, and therefore he may be able to return to ordinary life, with reservations or it may be that his morbid beliefs absorb all his mental powers and compel institutional life The more the psychiatrist can discover healthy modes of response in the illness itself as well as in the previous personality the happier the outlook Many patients, after an attack do not return to work but have narrower interests and less spontaneity than before, they are more easily tired and may be hypochondriac or show other symptoms thought to be neurotic " Such patients have sometimes made a poorer recovery than others who return to work and can meet most social demands, though careful enquiry reveals definitely schizophrenic sequelæ in their thinking and emotions

The simplest rule is that an abrupt onset of the illness an adequate cause for its occurrence and a well adapted non schizoid personality are the criteria of good prognosis Sensible early treatment may avert disaster

Treatment —PROPHYLACTIC —This, whether eugenic or individual, is limited and uncertain Even if effective, it can reach only a minority at present, and its effectiveness is a matter of faith Probably child guidance and other measures of mental hygiene do good in averting potential schizophrenia but no one can be sure of this Such treatment aims at diverting the child into social activities and keeping him out of situations in which he will be mortified or otherwise troubled emotionally However wordily or abstrusely the prophylactic treatment be described, it is essentially a matter of trying to make an unusual child into an average one or changing his surroundings to suit him

TREATMENT OF THE ACTUAL ILLNESS —There is no one treatment of the disorder that has manifest superiority over any other Insulin has striking results in some early cases but is neither a specific nor a panacea Painstaking attempts at readjustment of the patient s outlook and behaviour by means of suitable psychotherapy, occupation games etc are the most systematic and rational ways of making a permanent change for the better The co operation of the patient is here necessary and also the help of a social worker desirable who may do much to modify and arrange the patient s circumstances in the interests of his mental health *e g* getting him suitable occupation and schooling his relatives in a sensible attitude towards him Such treatment is not practicable for those acutely ill but for the mild the convalescent or the imperfectly recovered case it is of great value By means of it many patients can be discharged from hospital before they have settled into apathy or become unresponsive to the claims of the external world it is better not to keep a schizophrenic patient in hospital waiting for complete recovery but to get him back

general trend of the illness and their prognosis and treatment must be assessed accordingly

Besides the paranoid beliefs and attitude referred to in previous sections there are a number of instances of this unhealthy relationship between the patient and his surroundings which may be mild in their outward form easily understandable in the light of the patient s history and fairly responsive to treatment Some deaf people become distrustful misinterpreting what they cannot hear plainly and construing it into a jeer or an insult Sensitive and shy people are often troubled by doubts and shame as to their physical or moral worth and by projection attribute to others the dislike or contempt they do not acknowledge in themselves This occurs in youths who masturbate and suppose others to remark it and in old maids who believe men to be pursuing them but there are many varieties of shame and desire besides the sexual which lead to such ideas of reference or persecution The development of paranoid reactions of this sort is usually plain So is that of the querulous resentful type of reaction *e g* in the man who believes himself done out of his rights and who becomes a persistent litigant or writer of memorials Before judging such a man psychopathic the extent of the injustice he has suffered must be compared with the degree of his resentment and his relevant conduct Commonly the injustice is found to be fanciful or trifling and the man s sense of grievance immoderate so that he comes to believe there is a veritable conspiracy to wrong him and devotes most of his time to useless appeals or threats He may persuade his wife or his children of the justice of his complaints inducing delusions in them *i e folie à deux* etc Many such patients however never become deluded they are contentious about their wrongs and waste years perhaps in proclaiming them or seeking redress but they are well aware how other people regard them and what has actually happened Many claimants of compensation grousers old soldiers and unstable adherents of more or less cranky movements are to be placed here There is no sharp dividing line between these psychopathic people and the more or less normal often socially precious leaven who detest injustice and are willing to do much to defeat it

HYSTERIA

In hysteria symptoms of illness are represented by the patient for the sake of some advantage without his being fully conscious of this motive The form of representation will vary widely according to the circumstances that have provoked the illness the patient s experience of what the symptoms are that he is trying to represent and his somatic resources These factors presently to be discussed bear on the hysterical symptoms that simulate physical disease But it is impossible to restrict hysteria to this physical form The illness that is represented by the hysteric may be a mental one moreover it is not possible to consider hysteria without regard to the mechanisms of its occurrence which manifest themselves in the personality and are mainly psychological Hysteria is the most psychogenic of all illnesses Its recognition is therefore a double problem (1) exclusion of what may be called genuine illness *i e* of a recognised morbid pattern and (2) discovery of an adequate motivation To ignore either of these requirements is to court error since hysteria may occur along with physical or mental disorder elaborating upon it and mimicking it and on the other hand some physical diseases give rise to symptoms indistinguishable in their form and apparent psychological mechanism from those of hysteria

Ætiology—A hereditary factor is probable in many cases Thus a group of hysterics who were pathological liars were compared with the average population in respect of the proportion of their brothers and sisters who were in mental hospitals it was five times as many and of the parents of the group a sixth were psychopathic From these and similar figures it is not possible to tell the mode of transmission or

that in the present state of psychiatry the value of a new therapeutic procedure should be assessed not by the reports of enthusiastic pioneers, invaluable though their efforts and observations are, but by the outcome of a planned therapeutic trial in which uniform standards have been employed in the selection of cases the method of administering the treatment and the assessment of outcome also due regard must be paid to the choice of those control " cases with which the beneficiaries of the new method are to be compared

The insulin method consists in the induction of hypoglycæmic coma daily for not longer than 3 months It is seldom desirable to exceed sixty comas The coma is allowed to last a variable period according to the clinical condition If unduly prolonged, it may be difficult to terminate it by the usual method—the administration of carbohydrate through a nasal tube or intravenously Persistent or irreversible coma is the chief danger of the treatment about a sixth of those who pass into such a state die Because of this and other complications mostly avoidable the insulin method should only be used by experienced persons in a hospital adequately organised and staffed for the purpose The treatment is most effective in cases which would have a good prognosis for the attack if treated by other methods In a series of more than a thousand patients treated with insulin, 13 per cent recovered and were still well 2 years later, at which time there were also 14 per cent much improved Such figures are so much influenced by the choice of patients that they cannot easily be compared with the results of other methods In the main however they speak in favour of the insulin method if applied with discrimination skill and willingness to use other methods also, during the administration of insulin or afterwards Frontal leucotomy has been employed in otherwise intractable cases, and some patients thus treated have become easier to look after or fit to leave the mental hospital

The details of treatment whether in hospital or at home must be individual even in such matters as the allaying of excitement no uniform procedure, *e g* continuous baths or narcosis can be a routine measure When excitement is extreme disturbances in water metabolism and loss of salts may be combated by giving 5 per cent saline intravenously 300 ml every other day alternating with forced fluids During stupor general measures for ensuring adequate food (in some cases feeding by tube) cleanliness and evacuation of urine and fæces must always receive attention It has been found that various chemical agents such as carbon dioxide inhaled in a 30 per cent mixture with oxygen and sodium amytal will temporarily interrupt a catatonic stupor this finding accords with the metabolic changes reported in the condition but its therapeutic value is slight

PARANOIA AND ALLIED STATES

The words paranoia and paranoid are used loosely by many Kraepelin gave paranoia its modern meaning describing it as the endogenous insidious development of a permanent and unshakable delusional system with complete preservation of clarity and order in thought will and action If the illness cleared up if it showed symptoms of an organic affective or schizophrenic syndrome or if it was provoked by external happenings it could not be paranoia Thus delimited the condition is exceptionally rare so rare indeed that there is no use in having such a category Moreover cases that Kraepelin himself called paranoia have since become obviously schizophrenic The same is true of paraphrenia There is now no profit in thinking of paranoid states as syndromes in their own right so to speak and of the same order as schizophrenia or affective disorders They are on the same subsidiary level as stupor hypochondriasis anxiety and depersonalisation When met with they must be distributed according to the accompanying symptoms and the

emotionally charged out of which the patient s symptoms will bring him more or less overt but unacknowledged gain This gain need not be material and obvious and may run directly counter to such accepted values as health and ability to work One of the plainest instances of a partial unsubstantial gain is that created by an injury and the resulting insecurity and claim for compensation or pension hysterical symptoms flourish in such a soil and are usually influenced for the worse by repeated medical examinations Hysteria occurs among soldiers under active service conditions and can readily be fostered in them by injudicious measures

Pathology —This is almost wholly a matter of psychopathology It is true that disseminated sclerosis and many other organic diseases of the brain may be accompanied by hysterical symptoms but the association is not a constant one The psychological changes can usually be traced further back than the happening that provoked the illness often they are the continuation of normal tendencies of childhood that have been fostered and extended by ill judged upbringing The hysterical symptoms that appear as motor or sensory phenomena show the patient s readiness for the translation of experience into bodily symbols this is a special instance of the universal tendency for somatic representation of experience converting it into action It is the facility and exaggeration not the existence of this conversion mechanism that is characteristic of hysteria What is thus translated or converted into physical terms has been something painful and unacceptable the partial exclusion of it from consciousness repression' of it is therefore understandable in its physical symbolic form it is tolerable and may even be prized Identification with other people is responsible for the frequent imitation of symptoms and for the epidemics of hysteria Clearly the mechanism need not be limited to the production of physical symptoms though bodily structure and local weaknesses may conduce to this There can be hysterical phenomena such as the dissociation seen in fugues and so called splitting of personality which are instances of the exclusion of recent and remote painful experience from clear consciousness The wishes and fears that deviously attain outward expression as hysterical symptoms do not derive solely from the recent past though much of their strength may come from it It must be admitted that there are some hysterics in whom this psychopathology cannot be demonstrated and that such cases are among the most intractable

Symptoms —These may be divided into (1) sensory (2) motor, including fits and (3) quasi psychotic

The symptoms can be like those of any conceivable affection of which the patient has a notion The cruder his notion the less will his symptoms be like those of the simulated condition but after he has been demonstrated to a class or repeatedly examined he may better his notion and consequently his symptoms come closer to those of organic disease Or if he has had opportunity of seeing insanity his pseudo insanity may smack less of the stage than it otherwise usually does The range of hysterical symptoms is so great that to describe them all in detail would take inordinate space and there is no need to do so

The *sensory* or more properly the *perceptual* symptoms include clavus and globus hystericus blindness deafness and anæsthesia The two former are so common in all sorts of mental disorder especially those accompanied by anxiety that they are of little specific importance in hysteria enquiry as to their presence will often in these rather hypochondriacal patients lead to their occurrence The difficulty in swallowing reported by hysterical women may be associated with a strong disinclination to eat—anorexia nervosa it should not be confused with depressive anorexia or that of pituitary cachexia Any cutaneous disturbance of sensation that the patient has a notion of can be presented *e g* anæsthesia either mono or bi lateral, or of stocking and glove distribution and analgesia of any part The anæsthesia seldom corresponds to any nerve trunk nerve root or spinal segment unless the patient has had special opportunities of knowing With an anæsthetic hand objects may be

the nature of what is transmitted but only to infer a hereditary factor The occurrence of hysterical mechanisms in children, and their frequency in *healthy adults* especially after calamities or in unendurable conditions such as may occur in war suggest, however, that hysteria is potentially present in most people and that environment is more important here than heredity The combination of heredity and environment may result long before actual illness occurs in a *hysterical personality* This is not found in all patients who show hysterical symptoms but nearly all people of hysterical personality show hysterical symptoms Many of the features of this personality are socially obnoxious but other features are not and it is wrong to use "hysterical" as a depreciatory epithet for a set of qualities that one dislikes These people are unduly responsive to the situation they are in especially if by their excessive response they can fulfil wishes of which they are hardly aware or evade what is painful in the situation, instead of meeting it and disposing of it adequately Unsatisfied with their own capacities, they seek to cut a better figure than their endowment warrants and are constantly posing and pretending This like all their behaviour and aims here described is not done with full consciousness but with a more or less sincere ignorance or ambiguity of purpose it is not a question of deliberate deceit of studied histrionics or malingering In thus responding to situations and turning the response to some inadequate end the hysterical person is characterised by a lack of inner stability and of constant standards of behaviour, and also by a lability of affect and an exuberant fancy The fantasies normal in childhood are here seen in physically mature adults who like children can temporarily live their fantasies absorbed in this unreal compound of past experiences and longings yet not so wholly divorced from their real surroundings as might appear In an attenuated form this is evident when they almost unwittingly manufacture some situation according to their needs—literally ' making a scene —and enter into it emotionally with a rapidity and fervour impossible for more stable people Egotism and untruthfulness (pseudologia phantastica) may be pushed to the point of delinquency There may be a longing for prestige sympathy love or some other emotional relationship, which leads the hysteric to behave in a way strikingly out of keeping with his demeanour on other occasions the inappropriateness of his behaviour even at the time may be obvious to a detached onlooker, but is not always so Many of these people can use illness or well acted fantasies of illness to satisfy their hardly conscious needs they may also gain their ends by forgetting what it would be painful to remember Here again the onlooker may find it hard to tell how genuine or complete is this forgetfulness but the question is of little moment compared with discovery of the motive for the hypomnesia Hysterics are often regarded as unduly suggestible because they respond so readily or violently to situations and to people with whom they develop an emotional relationship often unrecognised by themselves as such The emotional attitude of a hysteric towards others is often influenced by sexual factors Hysterical personality is believed to be commoner in women than in men and may be associated with psychosexual immaturity Coquetry and frigidity are not uncommonly allied in hysterics there may be much flirting and sexual excitation stopping short of coitus It is however juster to say that the sexual lives of hysterics show instability and inadequacy than to specify any particular aberration

Hysterical personality can be recognised before puberty in younger children however it must be extreme to be recognised because of the great frequency of such mechanisms normally then (*e g* behaving as though fantasies were real counterfeiting illness somnambulism) Some of the grossest instances of hysterical behaviour have been recorded in girls not yet adolescent *cf* the Salem witches Much of the work of child guidance clinics is taken up with the treatment of hysterical tendencies not perhaps taking the form of definite symptoms but plainly evident in the child s personality

The precipitating factor for the onset of hysterical symptoms is usually a situation

They may be little more than a fainting attack or an outburst of temper, significantly like the tantrums of an ill behaved child Often however they are more differentiated than this and diagnosis from an epileptic fit may be difficult Sometimes the fit grows out of a tremor induced by fright or anxiety or it may express some emotional state such as great pain anger or erotic excitement Occasionally the patient shows plainly by her expression and movements that the fit is erotic it may be a typical orgasm The ' classical four phase fits which Charcot described were artefacts of the clinic, they do not happen now

Sometimes the patient s fit becomes very like an epileptic one after he has spent some time at a neurological clinic, or he may be an epileptic who also has hysterical fits Some hysterics by overbreathing induce an epileptiform convulsion which can be abruptly terminated if an injection of calcium chloride or gluconate be given They may pass from one such fit into another so that the condition suggests a status epilepticus The unconsciousness that often appears to accompany a hysterical fit is seldom as complete as it looks neither is the subsequent amnesia There may however be a delirium corresponding to the emotional upheaval Patients very rarely hurt themselves seriously in the fit however violent or have a fit when alone or asleep The length of the attack and its degree often depend on the audience, the more the bystanders try to restrain the movements the wilder do the kicking, struggling biting shouting panting spitting etc become and the longer they go on There is neither the pallor nor the cyanosis the regular sequence nor the subsequent headache and sleepiness of epilepsy, urine is not passed nor the bowels opened reflexes including the corneal response are unaffected and the end of the fit may be abrupt

The *quasi psychotic* symptoms are stupor, twilight state pseudo dementia and fugue In the stupor seen typically in harassed weary soldiers under bombardment the patient lies motionless taking food like a 12 months baby non resistive sometimes incontinent of urine or fæces and without any predominant emotional tone It is of brief duration if the exciting circumstances cease to prevail In less acute forms there may be a sullen resistive akinesia or a condition lasting even for years with an occasional break this is a rare form Only with great caution and reserve should such stuporose or semi stuporose conditions be regarded as hysterical physical factors often play a large part in causing them or they may be schizophrenic The confusional or delirious states may accompany a fit or represent an important emotional experience *e g* some sexual episode They are often histrionic and represent wishes of a religious or grandiose sort or the patient may behave as though he were an animal or a child Sometimes they occur during the night and in a somnambulist state the patient repeats some past happening or may do complicated work This is closely akin to the hysterical fugue in which there is not so much a clouding as a narrowing of consciousness a dissociation In the fugue the patient says he has forgotten some or all of his life before a certain date and later he may profess to remember nothing of what has happened during the fugue There is in short a double set of memories which may alternate and since the patient s own identity is commonly included in the repressed and temporarily forgotten material he may be said to have two personalities and sometimes three or four Actually there are no cases in which it is strictly correct to speak thus of multiple personalities it is only a matter of different aspects or fragments of the one personality In the fugue the patient may live out some fantasy or—as more commonly happens—simply says that he does not know who he is or where he lives Nearly always a hysterical fugue with gross amnesia turns out to have been a means of evading some predicament and it is well to keep in mind in such cases that the patient may have broken the law or otherwise exposed himself to disgrace and punishment The amnesia is seldom as complete as the patient states Fugues may occur as a hysterical mechanism in an organic psychosis for example in a man with arrested general paralysis who had been prominently and in detail reported as a case of multiple personality which

identified and any test which the patient does not recognise as referring to this disability he will perform satisfactorily Such tests are not a means of catching the patient out as though he were a malingerer, but of *ascertaining whether the symptoms express only his notion of some illness* The tests for a malingerer, it is true amount to the same thing though one assumes the malingerer to be clearly conscious of his purpose consequently any distinction between *hysteria and malingering must* depend on the observer's impression as to the patient s honesty and self knowledge certainly it cannot be decided by tests The tests for blindness (*e g* using a stereoscope with a supposedly blind eye) deafness (*e g* effect on pulse respiration and psychogalvanic reflex of exciting remarks addressed to the patient) and for other forms of perceptual defect all depend on the physician s greater knowledge of what should or should not accompany the symptoms of which the patient complains they are not intended to discover hysterical " stigmata or characteristic anomalies The ovarian and other hyperæsthetic spots the pharyngeal anæsthesia and the concentric limitation of the field of vision formerly used diagnostically were all products *of suggestion or, as in the last instance* phenomena that may occur in normal fatigue in hypochondria and in certain cerebral lesions

The *motor* symptoms are paralyses pareses spasms contractures and tremors Hysterical paralysis or paresis never affects individual muscles but always movements By various devices it can be shown that the patient can still use the affected muscles as long as he does not know that the movement in question requires their use The paralyses affect chiefly the left side of the body are common in the *legs* (preventing proper walking or standing) and often occur in limbs or other structures that have earlier been the seat of an organic disability *e g* trauma or paresis If the *paralysis be flaccid no loss of tone or of reflex response is found, and the patient,* through his ill informed notions of what should happen behaves otherwise than a patient with organic paralysis would—*e g* if asked to rise from the supine to the sitting *posture without using his hands he keeps his paralysed leg flat on the* bed If the paretic part be kept stiff the antagonists will be found to come into action first when the patient is asked to perform the movement he says he cannot and if the movement has to be made against resistance sudden removal of the resistance reveals how much of the apparently tremendous effort was going into associated irrelevant or antagonistic movements Passive movement to overcome the spasticity or subsequent contractures cause the patient to be more upset than could be accounted for by any pain he may complain of The varieties of abnormal gait are numerous many of them fantastically elaborate and from the look of them exhausting Not only the musculature of the limbs may be affected but of the trunk (leading to curvatures and odd postures) and indeed any voluntary muscles *e g* of the tongue larynx pharynx or eye In hysterical aphonia the voice may sink to a whisper or there may more rarely be complete mutism the voice can however be used normally for coughing and similar purposes *The aphonia often comes on after some local inflammation* that has caused hoarseness or after a fright. Stammering usually of the exaggerated kind may also occur Spasm of the external ocular muscles leading to a convergent squint *may accompany a spasm of accommodation* Ptosis and blepharospasm sometimes occur Many of the tics and spasms that used to be thought hysterical are now recognised to be often physiogenic, *e g* residual symptoms of encephalitis *lethargica and chorea* spasmodic torticollis for instance is far less often psychogenic than used to be supposed When a spasm or paresis has long been maintained trophic disturbance may follow blueness and œdema shiny skin fibrosis of periarticular structures and similar effects of rigidity and disuse Tremor may occur and is often gross as in many of the war cases It is variable in degree and *rhythm and often* disappears when the patient s attention is turned from it this however is not a safe criterion

Hysterical *fits* commonly occur in patients with obviously hysterical personality

of some physical disease It is however in neurology that the most difficult cases of all arise e g in disseminated sclerosis carbon monoxide poisoning cerebral vascular disease or encephalitis lethargica here there is more likelihood of the organic disease being overlooked than of its being wrongly diagnosed The patient s previous personality any provocative situation or emotional disturbance the previous occurrence of organic signs e g transient diplopia and the age of the patient must be considered Hysterical symptoms appearing for the first time in middle or later life in someone whose personality has been stable are probably not solely psychogenic If the symptoms diminish when little or no attention is paid to them they are more likely to be hysterical

Course and Prognosis —This depends mainly on the patient s personality and social setting and on the treatment employed A long history of hysterical traits prior to the illness a continuance of circumstances favourable to the symptoms and inadequate or excessive treatment are all unfavourable This is however an illness that sometimes confounds prediction patients recovering when many adverse factors have been operative and the symptoms have been present for years In children the prognosis is fairly good if treatment can be undertaken promptly it is best if the hysteria is monosymptomatic and has come on after a fright In all cases in which the situation which provoked the illness persists the outlook is bad for example in compensation cases for which no medical treatment is of any avail—for obvious reasons—until the litigation is settled once and for all Similarly during war psychotherapeutic successes are often dazzling while the hysterical soldier is under treatment in hospital but the symptoms come again when he must return to duty There are many varieties of outcome chronic invalidism being the commonest A few patients later become schizophrenic and a few become involutional melancholics The prognosis in respect of the patient s hysterical personality is more important than that of his hysterical illness it is however no more to be assessed by rules than the general future of any human being s life and personality Patients do not necessarily tend to become anti social delinquency is certainly a likelihood in some hysterical people but bravery and self devotion may be conspicuous in others

Treatment —Too much treatment is worse than too little Injudicious physical or psychological treatment of hysterics often makes their symptoms worse and their illness intractable Recondite methods should be eschewed by all but experts Common sense is as important as psychological understanding and social usefulness more to be aimed at than removal of symptoms or attainment of self knowledge In short it is not the hysterical illness or the mechanism of repression and conversion that calls for remedy but the patient s inadequate way of dealing with difficult situations Consequently the whole treatment must aim at the patient s return to ordinary conditions of life as soon as possible and at a re education of his ways of meeting difficulties To this end it is profitable to go over with the patient the situations emotional disturbances and motives that led up to the illness and to do this without implying moral judgement or social indifference—certainly without teaching the patient one s psychological theories It is a matter of general psychotherapy (see p 1619) and it may entail a far reaching analysis of the patient s past life her emotional development and her instinctual tendencies It is questionable however whether anyone without special psychiatric experience is wise to enter lightly upon this way of benefiting the patient For on the one hand he may be misled into a wilderness of fantasy masquerading as once repressed now recalled psychic trauma and on the other he may be at a loss how to deal with the attachment and dependence upon him which the patient will come to show and which may in fact be the chief influence in bringing about her precarious recovery A great deal may be achieved—perhaps as much as by more thoroughgoing methods—if the physician himself mature and with impartial insight into the psychological motivation of the symptoms leaves aside in his dealings with the patient any very detailed enquiry into the more remote

responded to psychotherapy Psychogenic fugues are not invariably hysterical, they may be symptoms of a reactive depression in which despair and perplexity are conspicuous

'Pseudo dementia" covers the large group who behave as though insane It may occur, as in the so called Ganser syndrome, *in prisoners awaiting trial* Whatever the circumstances, its motive is escape from a disagreeable situation It is likely however that it is mainly those with a predisposition towards severe mental illness especially schizophrenia and the high grade defectives who have recourse to this *kind of hysterical behaviour* It sometimes comes on after brain injury The patients behaviour corresponds necessarily to their notion of insanity which is usually far enough removed from anything the psychiatrist knows as such Occasionally, however, it is very near the buffoon like conduct of some schizophrenics The patients say that they do not know their own age affect not to understand simple remarks give absurd answers which nevertheless indicate that they know the right answer (*e g* by inverting the correct order of the figures in a sum) When asked about some simple matter they look as though they were making terrific efforts to remember (herein behaving differently from the schizophrenic) The most characteristic thing is the disparity between the patient s alleged deficiencies and his general alertness he says he does not know anything about his own past, he cannot read or spell or do the simplest arithmetic and yet he may be behaving quite naturally and adapting himself to the situation in a way which would be inconceivable if he had actually so advanced a dementia

Some hysterics go to great lengths in their representation of ideas of illness They will allow *themselves to be put among grossly insane people or submit to repeated* operations, such as amputation Self inflicted injuries *e g* keeping wounds and sores open are not uncommon (cf dermatitis artefacta) In some such cases masochistic tendencies can be recognised but by no means in all Suicidal attempts are not *infrequent They often have as their purpose revenge the satisfaction of some spite*, and the patient may leave behind a lying fantasy coloured letter, indicting someone Frequently the suicidal attempt is in the nature of a theatrical demonstration, carried out in such circumstances as make it unlikely to be fatal, and if the patient kills herself, it is more through bad management than intention

Diagnosis—It will be plain from what has been said that diagnosis must be both negative and positive—negative, by excluding any organic cause for the symptoms positive, by finding motives and relating the symptoms to them Neither method is alone sufficient because of the occasional concurrence of structural disease with psychogenic symptoms As to the former *i e* the negative method it is unnecessary to enter here into all the differentiating points Many of them have been mentioned in the foregoing description of symptoms and all turn on the disparity between what experience tells us would occur if these symptoms were of organic origin and what the patient knows about such matters Consequently a doctor who has hysterical symptoms is extraordinarily difficult to diagnose in this negative sense The method of arriving at a diagnosis by suddenly taking the patient unawares and seeing if his symptoms persist is to be deprecated it antagonises him Likewise undesirable is the procedure of seeing whether one can suggest new symptoms to the patient *e g* an anæsthesia, it can be both misleading and harmful Neither is the hysterical nature of a symptom to be judged solely by whether it can be removed by suggestion for some organic symptoms are temporarily got rid of thereby and many *hysterical* symptoms are not An intimate knowledge of the range of symptoms of physical disease is much more useful to the physician than an equipment with special tests and lists of differences between functional and organic It is not only a problem of neurology but of the whole of medicine since the hypochondriacal tendencies of many hysterics lead them to complain of visceral symptoms usually in doubtful cases, the symptoms are those which might well occur in the earlier stages

Marriage should never be recommended as treatment for hysteria the superstition about this has resulted in lamentable troubles especially for the person the hysteric marries This is not to say that every hysteric is to be dissuaded from marrying there are more things than treatment to be considered then Married hysterics, however should not be recommended to have—or to adopt—a child Contrary to popular notions pregnancy and puerperium more often aggravate than benefit hysteria Moreover hysterical women are not usually satisfactory parents and commonly induce psychopathy in their children

ANXIETY STATE

As already stated the emotional syndrome so called is part of the group of affective disorders in which depression and manic excitement are also included It is there described It would be indefensible to put into a special category all the forms of mental illness in which anxiety is conspicuous for it can be severe in the most diverse conditions ranging from delirium tremens to schizophrenia The outwardly mild form tending to chronicity and often largely psychogenic responds well in the less advanced stages to psychotherapy it is therefore important that its recognition should not be delayed because of a doubt as to physical disease Yet often the correct diagnosis is overlooked while the patient is being investigated or treated for some local disorder This arises partly because of the quasi physical signs of fear which he may show—dizziness tremor nausea and vomiting indigestion diarrhœa palpitation a sense of oppression in the chest rapid pulse flushing sweating frequent passage of urine etc It is still more due to the patient s anxiety turning on his health especially his physical health and leading him to ask for more and more medical opinions radiograms laboratory investigations etc the favourable results of which however do not allay his worry Over cautious advice as to régime based on a possibility that there may be some early physical disease can be harmful to the patient s mental health in that it restricts his normal life and may constantly recall and reinforce his anxiety The converse error of mistaking some early symptoms of physical illness for hypochondriacal anxiety is equally to be avoided Physical investigation of doubtful cases is in short indispensable and should be prompt as well as thorough When it fails to confirm the presence of a physical disorder the patient should not be treated as though he will still be in danger of the physical illness unless he takes special precautions in diet exercise etc This is well illustrated by such a condition as effort syndrome where care taken to avoid any damage to the heart intensifies the illness The patient should be fully investigated on the psychological side and treated accordingly this does not mean that he should be treated only by psychotherapy The discovery of a possible psychological cause for the symptoms does not prove that there is not also a physical cause for them but it makes it less likely The converse is also true For ætiology diagnosis prognosis and treatment see section on Affective Disorder (pp 1645 to 1651)

OBSESSIONAL DISORDER

Definition —In this condition the characteristic feature is that along with some mental happening there is an experience of subjective compulsion and of resistance to it Commonly the mental happening (which may be a fear an impulse or a preoccupation) is recognised on quiet reflexion as senseless nevertheless it persists

Ætiology —INTRINSIC —The hereditary factor is strong A third of the parents *of obsessional patients and a fifth of their brothers and sisters have themselves* shown pronounced obsessional traits the proportion is in each case higher if all forms of mental abnormality be included since both schizophrenia and affective illnesses occur

causes of the illness and the purposes it served, and instead directs her towards a better social adaptation by advising her to avoid when possible the situations that, as he sees favour the production of symptoms getting her into a disciplined way of living and stepping in with explanation support and advice whenever fresh difficulties arise His success in getting rid of individual symptoms at the beginning may be an important factor in establishing the necessary relationship with the patient Such a line of treatment is not heroic or dramatic and it demands a great deal of the physician but it avoids some of the commonest blunders and may be strikingly successful For this or indeed any treatment admission to hospital is not essential but it will help when there are adverse factors in the patient s situation and of course will be essential if there be such symptoms as self injury, suicidal attempts pseudo dementia or gross paralysis The danger of the patient s picking up new symptoms in hospital should also be weighed Isolation is usually inadvisable

Many of the symptoms of hysteria will not wait upon general treatment but demand energetic intervention Anorexia for instance, cannot be allowed to go on to an avoidable inanition nor a paralysis to the stage of contracture a mute patient or one who is deaf or blind or ignorant of his own identity, offers such practical obstacles to almost any kind of treatment that the symptoms must be tackled and disposed of early For this purpose suggestive measures are valuable and appropriate physical treatment may be called for *e g* supervision during feeding or even tube feeding in anorexia nervosa physiotherapy for paralysis, voice exercises Suggestive measures need not take the form of hypnosis suggestion in the normal waking state has many advantages over hypnosis though those expert in the latter are sometimes very successful in their treatment Suggestion like almost every form of treatment of hysteria has pitfalls and its triumphs like those of every other method sometimes prove vain but in the hands of a physician who is at once confident and cautious this method may result in a satisfactory recovery If in using suggestion such physical devices as faradisation can be avoided it is better to do so As a means of demonstrating that the illness is not due to local disease however such methods sometimes take their place in a detailed plan of treatment Motor and sensory symptoms can usually be got rid of if the physician is patient determined and confident in the use of persuasion and suggestion Intravenous injection of a barbiturate such as sodium amytal may facilitate such treatment and may help the patient to disclose motives and happenings he had been reluctant or unable to talk about disclosures of this kind however must be received and utilised with caution and lasting benefit is not to be expected from such catharsis alone

The choice of occupation the settlement of any social cause of illness (*e g* claims for compensation) and the obtaining of a healthy attitude—neither complaisant much enduring nor harsh—on the part of the patient s relatives and friends are all important factors in treatment The hysterical reactions to injury call for special mention because of their frequency Though often of transparent motivation they are not by any means to be regarded as outright malingering for the patient s feeling of illness may be sincere his symptoms distressing his anxiety typical and his irritability and insomnia symptoms that he would gladly get rid off But they are none the less psychogenic It is often assumed that so far as an illness is psychogenic it must be treated only by psychotherapy This is false theory There are few mental disorders in which psychotherapy alone produces such small benefit as in the hysterical conditions due to the compensation or pension situation that may follow an injury Putting an end to the situation early and the resumption of ordinary activity as soon as any physical injury has been repaired are the most potent measures in the earlier stages Even if the symptoms have been present a long time the ending of disputes about claims and the return to ordered routine and regular occupation achieve more than do frequent medical interviews Psychotherapy is then an adjunct not an essential feature of the treatment

some forgotten alarm and take a queer form such as a phobia of lavatories or of one legged men It is loose usage to give the name phobia to every case in which an individual develops fear that is excessive or inexplicable, the essential features of an obsession already mentioned should also be present The term claustrophobia for example is often loosely applied to a fear or dislike of being in an enclosed place which is not obsessional Fears of dirt or infection are very common phobias they are symbols of moral usually sexual taint, and they lead to much washing etc thus a patient who has blamed himself for masturbation may be constantly washing his hands or following a complicated ritual of touching nothing with his bare hands for fear of contamination Often the rituals and defensive precautions seem grotesque when compared with their ostensible purpose as in the case of a patient who is perpetually putting himself to the greatest trouble in order to ensure that he never steps on a worm inadvertently Ludicrous as his behaviour may seem it is often tragic in the distress and indeed ruin it may cause him Another phobia is that which has fear as its object *i e* the patient is afraid of any situation in which he may feel fear some such patients do not leave their homes for years because they fear they may have agoraphobia once they get outside Obsessional *rumination* usually takes the form of endless questioning or search The patient has to ask himself Why with pointless insistence about all manner of problems beyond his or anybody s grasp or he has to keep casting round in his mind after some forgotten name or word which he could easily do without Religious scruples sometimes fall into this category as when a penitent is continually running to his confessor with some venial trifle he has come upon in his interminable self questioning and doubt

Obsessional patients are in most cases depressed, their illness is a depressing one Besides this secondary depression, however there is frequently an association of a more intimate kind in which depression—or mania—is the essential or the main part of the illness and the concurrent obsessions seem to be symptoms of this affective disorder In such cases the obsessional illness is very often cyclical in its course Anxiety is a common accompaniment of obsessions in phobias it is most conspicuous The anxiety is inseparable from the patient s struggle against the subjective compulsion which is so alarming to his feeling of integrity in self and mind such a shock to his belief that he is a free agent Schizophrenic symptoms may be in the offing or actually present when the obsessional ideas are of the magical kind *e g* the patient feeling that the effect of his obscene thoughts upon others may be averted by some gesture or when his rituals are carried to bizarre lengths *e g* having to save the last drops of his urine because of some recurring doubt Depersonalisation may occur in the course of an obsessional illness

Diagnosis—If the essential features *i e* feeling of subjective compulsion and immediate resistance to this be kept in view it is seldom difficult to distinguish between obsessions on the one hand and delusions hallucinations ideas of reference or self reproach feelings of being influenced and schizophrenic stereotypies etc on the other The only difference between obsessions and many schizophrenic phenomena towards which the patient retains insight and which he regards as alien to him lies in the nature of the compulsion he experiences in obsessions it is subjective—he feels that it comes from within his own mind, whereas in the schizophrenic phenomena he feels that it comes from without it is imposed upon him It is a difference however that may be obliterated *i e* what was once obsessional may become schizophrenic but this is an uncommon outcome when the obsessional disorder is definite and well established In differential diagnosis it must be remembered that obsessions may occur in the course of almost any mental illness in a person of obsessional tendencies and that the psychological mechanism for the production of obsessions like that for hysterical symptoms is present in almost everybody in varying degree Consequently an illness is not to be regarded as obsessional unless obsessions are the chief symptoms

with more than average frequency in families of obsessionals The abnormal personality of the parents is probably also potent as an environmental cause Very many obsessional patients have for years before they became ill shown a rather characteristic mental constitution they are excessively cleanly orderly and conscientious sticklers for precision, they have inconclusive ways of thinking and acting, they are given to needless repetition Those who have shown such traits since childhood are often morose obstinate, irritable people others are vacillating uncertain of themselves and submissive Obsessional traits occur however in many people who never become mentally ill and in many who become mentally ill otherwise than with an obsessional disorder Consequently these traits cannot be rigidly held to be the forerunners or non morbid counterparts of obsessional illness

EXTRINSIC —The influence of strict morose cruel overconscientious or obsessional parents has just been mentioned It is difficult to weigh its importance certainly in some cases it plays no part There is nothing specific in the situations which supply the content of an obsession they might equally well have preceded hysterical symptoms for example in a person so predisposed Nevertheless, the fright or pain which once accompanied a particular experience or a long series of experiences must not be overlooked in working out the multiple causes of some obsession psychologically related to this experience

Encephalitis lethargica and a few other cerebral diseases may produce typical obsessional symptoms in persons previously free from demonstrable tendencies in this direction

Pathology —Apart from the difficult instances in which lesions of the brain are accompanied by obsessions, this is at present wholly a matter of psychopathology Some elements of an obsession are universal human attributes all little children tend to ritualise and repeat all human beings are at times uncertain of the rightness or sense of what they have done they try to avert trouble by symbolical acts and other magical devices whose effectiveness they may question (*e g* superstition), many normal people moreover have mild obsessions that do not bother them (*e g* scruples) The manifest struggle going on in the obsessional patient may be restated in terms of hypothetical instinctual tendencies Such attempted explanation cannot be verified, and it is more useful to pay heed to the repression, displacement and substitution which lead to symbolic representation of emotionally significant earlier experiences and to the protective mechanisms by which the patient tries to ward off the painful and overwhelming obsession with the result that he develops complicated rituals and similar devices which may be mistaken for the essential symptom The transition from obsessional to schizophrenic is easy to understand psychopathologically since in both some contents of consciousness are separated from the main stream

Symptoms —Obsessions are conveniently classified as (1) ideas or images, (2) impulses (3) phobias and (4) rumination These overlap constantly

Among obsessional *ideas and images* are tunes, phrases mental pictures of a disagreeable sort (*e g* of a mutilated corpse) and obscene associations (*e g* every cranny reminds the patient of a vulva) Obsessional *impulses* are often of a suicidal or aggressive character the patient may feel an urge to kick people in the street to push his friend over a cliff or to throw himself under a passing train In many other cases however, they are less alarming *e g* impulses to swear loudly in church or to laugh at a funeral or more of an intellectual sort such as an impulse to count and manipulate numbers senselessly or to avoid typing any word with a given number of letters or beginning with a particular consonant *Phobias* are closely bound up with the other varieties of obsession thus the patient who has an impulse to plunge a knife into his friend s or his own neck has an understandable phobia of knives the patient who is troubled by obscene thoughts whenever he looks at a naked statue develops *a phobia of museums* Not all phobias can be so accounted for, they may rest on

sometimes themselves In this it is like mental illness and calls similarly for psychiatric understanding and treatment But since they are not ill their behaviour must be attributed to abnormal personality, much as an aberration like alkaptonuria must be attributed to abnormal physical constitution All abnormality of personality that does not amount to manifest illness may properly be called psychopathic personality The term does not connote an evaluation of character according to how useful such a person is to society, nor is it a prediction about the likelihood of subsequent illness of a particular type, it is a descriptive term But people of abnormal personality will often come into conflict with organised society and with individuals more normally constituted they will be on the whole more vulnerable to stresses, their peculiarities intensified into symptoms of illness or proofs of delinquency will earn them pity contempt dislike punishment or compulsory treatment It is therefore common for ' psychopathic personality to be used as a pejorative term limited to those who will afflict society in some way—the anti social psychopath , the psychopathic tenth are significant phrases akin to psychopathic inferiority and the still earlier moral insanity or the term is used to denote those who stand in danger of insanity—the schizoid psychopath for instance It is however wrong to apply to the concept psychopathic personality so shifting and subjective a criterion as social disapproval nor can mental illness be assumed to be a certain outcome in even pronounced aberrations of personality Among mystics and poets men of action scholars and scientists are some who have properly been classified as of psychopathic personality , their abnormality consisting nevertheless in unusually high rare and valuable if peculiar qualities rather than in a blemish or handicap St Teresa Joan of Arc T E Lawrence Cavendish Cellini Tolstoy Mozart, Michelangelo—any hurried list of famous people that have been cited as examples of psychopathic personality testifies to this Apart therefore from any judgement about the good or harm they do to society people are said to have a psychopathic personality if they fall outside the wide range agreed upon as normal—not quite the same thing as healthy—yet are not ill Society being ordered as it is the majority of such abnormal people will at some time come into conflict with it or fail to meet its demands and their conduct will often rightly be called anti social The anti social group of persons with psychopathic personality is large its size will vary according to the culture in which they live and the allowances or opportunities it makes for them This is obviously true if their adjustment as adults to the demands of the community is the measure of their anti social trends it is true also of their development and the way in which social influences may be such as to foster their smooth participation in a very diverse pattern of human relationships or may mar them giving neither free play nor direction to their peculiarities Success in preventing many of these abnormal people from becoming a nuisance or a danger is therefore a test of the educational methods the pliancy and the psychiatric hygiene of a community This is not to ignore the hereditary and narrowly individual factors which determine psychic constitution but to stress the social causes of later social failure should it occur such failure however, need not be regarded as inevitable in people of psychopathic personality

Classification of psychopathic personality can be (1) arbitrary (2) psychological or (3) psychiatric The first picks out what seem serviceable characteristics that occur often and conspicuously thus one well sponsored list is made up of the excitable the unstable the impulsive the eccentric and perverse the quarrelsome the anti social and the liars and swindlers and makes further reference to æsthetes scatterbrains enthusiasts and fanatics The second which is the ideal method is based on the varieties of normal personality Unfortunately the types trait-clusters and other classificatory groups so far proposed do too little justice to the complexity and range of human personality to be satisfactory or lasting The third or psychiatric classification is likewise provisional but it has the advantage of grouping

Course and Prognosis —The outlook for recovery is worse if obsessional symptoms have been present since childhood if they now fill up most of the patient's time, and if he is weakly *resigned to his illness* *The best outlook* is when the obsessional illness comes on suddenly in a person who has not had conspicuous obsessional traits or who has had previous benign attacks A cyclical course is not uncommon The situation is ominous when the ritual gets more and more systematised and remote from what previously occasioned it The development along schizophrenic lines already mentioned, is more to be feared in such cases and in those with bizarre obsessional thoughts, the great majority of gross obsessionals however do not *become schizophrenic or anything else than obsessional* About *half* the cases recover from an attack which may, however, last for a year or even more Many people are subject to brief attacks lasting only a few days and largely due to fatigue or physical illness reducing their mental health Intercurrent happenings influence the course of the illness *e g* some men were free from symptoms during their period of war service with its routine and lack of responsibility or need for decision The content of the obsessions is of little use prognostically Old age is not in itself an adverse *factor but attacks in childhood suggest a strong constitutional bias and are therefore* unfavourable on the whole Few obsessionals give way to anti social impulses *e g* to suicide homicide delinquency It is true that obsessionals who are also depressed may kill themselves, and that obsessionals who are irritable and angry may injure others, but obsessionals rarely yield directly to an impulse they have resisted or need to have ' irresistible impulse urged in extenuation of a crime Sexual offences and perversions are rarely obsessional

Treatment —*Patients should be encouraged to continue at their occupation and* not to test themselves, or try to overcome their obsession, by repeatedly putting themselves in a situation in which it will occur So long as their impulses are not likely to get them into trouble they should be dissuaded from 'fighting' them external restrictions are more helpful than reliance on will power The physician should aim at getting a patient well by putting an end to his anxiety and struggle, if that is not wholly attainable the patient must be educated to deal with his obses*sional tendencies by acknowledging their existence their psychological origins* and often their harmlessness in those very respects in which he thought them most harmful, *e g* obscenity Frank recognition of obsessional tendencies which everyone has in some degree is an important step in learning to control them In some patients the obsessional attack is so cyclical and almost self limited that a brief rest and general care are all that are needed In others whose affection is chronic recovery is out of the question but advice about the management of their lives varying according to *their individual circumstances helps them greatly* In some such patients frontal leucotomy lessens or removes the distress that formerly accompanied their obsession Obsessional patients so prone to rumination and endless questioning often clamour to be psycho analysed There is no evidence that psycho analysis however prolonged benefits them more than methods that are not so exigent of *time and money* Obsessional children who may be beset with fears of contamination and religious scruples usually respond well to changes in their human environment advised after the physician has enquired into the family and school situation temporary separation from an obsessional parent or treatment of the latter often proves remarkably beneficial for the child Discussion of his problems with the child is an important adjunct of such treatment, just as it would be with an obsessional adult

PSYCHOPATHIC PERSONALITY

There are many who do not regard themselves as *ill nor do others think* them so yet their behaviour is abnormal enough to upset or puzzle other people and

and feeble mindedness begins Again as with mental disorder the same clinical picture may be due to a variety of causes ranging from heredity to trauma They are moreover delimited rather by social than by other criteria and they are not definitely associated with any constant pathological findings except in the numerically limited group of special clinical types In that they are capable of only limited improvement when well established and that the intellectual functions are more obviously damaged than any others their similarity to cerebral impairment in adult life is easily seen They are not by any means cases of purely intellectual defect they represent, it is true one extreme on the scale which has people of great intellectual ability at its other end but they are also examples of a general impairment of mind affecting the emotional and conative functions and often associated with a more general impairment of the whole organism, which may be seen in its physical structure Since the milder forms are indistinguishable (except on an arbitrary reckoning) from what may be termed normal stupidity it is difficult to use rigorously the official definition of mental defect as a condition of arrested or incomplete development of mind existing before the age of 18 years whether arising from inherent causes or induced by disease or injury but the description is serviceable It should be recognised that just as psychosis differs from neurosis only in a rough social sense turning on the need for special care and neurosis from normality only in respect of the limitations the former imposes on one s daily life as a social organism so does the distinction between normality and feeblemindedness and between gross or certifiable deficiency and the lesser forms turn on the social adaptation of the person in question To complete the points of similarity there is recognised a ' moral defectiveness which has its parallel in some kinds of ' psychopathic personality The effects of encephalitis lethargica parenchymatous syphilis and thyroid deficiency upon the mental state and development at different ages or the varying results of amaurotic familial idiocy in the infantile and the delayed juvenile form illustrate how important is the stage of growth or maturity at which damage is done

Ætiology—The customary division is into primary (hereditary) and secondary forms but a less dogmatic distinction is between those who represent the lower extreme of normal variation (the subcultural group) and those in whom a gross structural pathology is discoverable The former group is a large one making up approximately three quarters of all cases of mental defect This is an estimate arrived at by independent workers but it may have to be changed as we acquire better methods of determination and fuller knowledge of the subtle interplay between environment and heredity The grosser the deficiency the less important the hereditary factor except in some rare well defined anomalies such as amaurotic idiocy Familial concentration of a given form of defect is specific for each clinical type A combination of several genetic factors is probably responsible for all but the special types the mode of transmission of amaurotic familial idiocy and of phenylketonuria is recessive that of epiloia dominant

The environmental causes are prenatal congenital or infantile they include birth injury to the brain meningo encephalitis hydrocephalus cerebral syphilis Various poisons and deficiencies may be responsible, as in the well known instance of cretinism as well as certain malformations of the cerebral tissue *e g* microgyria and porencephaly, and of the cranium *e g* oxycephaly The influence of maternal rubella and other exanthemata and of Rh incompatibility upon the fœtus have lately been studied in this connection Sensory defects as in a deaf mute may greatly impair mental development It is possible that some cases of schizophrenia beginning in the first few years of life are indistinguishable from mental defect and are diagnosed as such

Pathology—In many cases there are no significant findings this is particularly the case with high grade defect It is probably impossible from the histological appearances to infer the extent of hereditary or exogenous causation Develop

these non morbid abnormalities in the same categories as the severe morbid ones (with which there is reason to believe them genetically connected) To do this begs some fundamental questions but it is for the present useful to recognise schizoid affective, paranoid obsessional hysteric and perhaps epileptic varieties of psycho pathic personality This list is open to the objections that must be made to any attempt at stating types of personality, and it is wrong to suppose that any of the varieties mentioned must always precede, or indicate proneness to the illness from which its epithet is derived Nevertheless they give the psychiatrist a familiar frame of reference and they leave room for manifold combinations of traits and attitudes within each class so that the individual drug addict the sexual pervert the hypo chondriac and the fanatic can be included If this psychiatric classification were to be judged by as rigorous a standard as the psychological it could not stand it will no doubt eventually give way before a surer psychology of personality and a surer psychopathology, as indeed it would have to now if the psycho analytical conception of the structure of normal and morbid personality were accepted as final For the time being it is convenient to use these derivative terms such as schizoid and to give them no more weight than the bare labelling of personality deserves Under standing a psychopathic person s motives and conduct of course requires full consideration of his development circumstances and traits and goes beyond their classification for clinical purposes

Besides the hereditary and social causes of psychopathic personality anomalies of cerebral structure may contribute to the condition But in childhood and even in maturity damage to the brain by infection, poisoning malnutrition or trauma can lead to changes in personality such as occur after encephalitis carbon monoxide intoxication, pellagra operations and accidental violence to the brain They do not conform to a single pattern and may be complicated by intellectual impairment They depend to some extent on the part of the brain affected, in perhaps the most striking group—encephalopaths whose emotional control is much reduced so that they easily become violent when they cannot get their own way—the hypothalamus and other structures in the rhinencephalon are suspect Electro encephalographic data have recently been added to the clinical psychological and experimental evidence for this Some writers believe that most of those with psychopathic personality characterised by violent outbursts have an innate or acquired cerebral abnormality and even though on inconclusive grounds that there is a kinship between the aggres sive psychopath and the epileptic It would however be a mistake to attribute psychopathic personality even when marked by excitability and impulsive acts of violence mainly to anomalies of cerebral constitution emotional deprivation or insecurity during childhood parental mismanagement and in adult life severe frustra tion and adversity constitute psychological causes which are often in evidence

Any description of forms of psychopathic personality must be lengthy as must also any consideration of their psychopathology and treatment Crime juvenile misbehaviour habitual or sporadic drug taking peculiarities of sexual desire and practice incapacity for certain occupations and public duties (*e g* school teaching military service) the temperamental concomitants of inferior intelligence and at the other extreme some of the characteristics of genius these are intimately linked with the problem of psychopathic personality, and their exposition would demand a fuller treatment than space allows

MENTAL DEFICIENCY

As already stated (p 1626) there is nothing in principle to separate these from other forms of mental anomaly save that they occur at an earlier stage of life Like mental disorder they shade into normality no man can say where stupidity ends

ways suggestible and accessible to flattery they may be obstinate and egotistical and readily fall into anti social courses e g prostitution vagrancy, crime Crude sexual offences or murder may be committed as lightly as some minor deception The personality of imbeciles varies widely some are docile and kindly others rough or deceitful and vindictive It depends much on their upbringing It has been found that in satisfactory conditions only about 8 per cent of defectives show anti social or troublesome behaviour But though the deviations of personality may not lead to delinquency, it is common to find in mentally deficient persons defects of tempera ment and character as well as of intelligence which are reflected in social inefficiency This is most important in the feeble minded who have intelligence enough to learn an occupation whether they can earn their living by it will depend on their character and the way they have been brought up

Many persons who are high grade defectives when measured by formal tests are not taken to be such because of their social adaptability, their fluency and capacity for keeping their heads above water as long as economic and other stresses are light There are instances of people classed as mentally defective during childhood because of their backwardness in school and their low score in tests who later in life amass money by their own efforts or even hold responsible positions A majority of high-grade defectives however live dependent and often troublesome lives at most they do simple repetitive work Many of them are unstable creatures whose psychopathic personality may be sufficiently anti social for the term moral deficiency to apply to them Hysterical trends may show themselves in crude phenomena e g con vulsions counterfeit insanity or fantastic lying and religious and artistic pretensions may take in gullible followers and even lead to the founding of ephemeral movements

Defectives are prone to disturbances of mood sometimes arising out of awareness of their inferiority and its social consequences Sudden outbursts of excitement may show similarity to manic or catatonic hyperkinetic states they may be accom panied by a paranoid hallucinosis mainly auditory which clears up with startling rapidity in a day or two In respect of these psychotic episodes defectives are like epileptics and juvenile encephalitics in whom a cerebral impairment has likewise occurred before the attainment of maturity Some of the morbid phenomena espec ially in idiots are very similar to the disorders of motility seen in schizophrenics because it may be assumed the same bodily mechanisms are implicated

The *mongoloid* type of defect is characterised by striking physical features Prob ably the outcome of intra uterine conditions it is most frequent in last born children in a large family or in children born of elderly mothers parental syphilis may occa sionally be the cause In many cases the brain stem and cerebellum have been dis proportionately small and other signs of maldevelopment have been reported Cere-bral metabolism is abnormally low It is likely that hereditary factors of an irregularly dominant nature also play a part The condition is usually present from birth physical growth is slow and has stopped by the time the child is 15 Defective growth of the skull leading especially to abnormalities of the base and the orbit are respon sible for the peculiarities of cranial shape The pituitary gland has been reported as showing an increase in eosinophil cells and deficiency of basophil cells The appearance of these usually happy idiots and imbeciles is rather suggestive of a Mongol or of a fœtus The skull is small and round and the junction of occiput and back of neck flat an epicanthic fold across each inner canthus narrow tilted eye slits and lids without lashes red cheeks fissured and often protruding tongue stubby depressed nose with nostrils looking forward irregular late appearing teeth coarse hair on the scalp small facial bones and occasional neurological anomalies such as nystagmus make the head of every mongoloid a disagreeable but ready index to his disorder That the disorder is a general one the rest of his body testifies his limbs are lax and over mobile at the joints he has broad clumsy feet and hands (with short fingers a special pattern between the base of the third and fourth fingers and a crease

mental anomalies such as general hypoplasia and microgyria may, however be mingled with evidences of a past lesion as in porencephaly or hemiatrophy or with signs of a disease actually present as in amaurotic idiocy cerebral lues and tuberose sclerosis Localised lipoid deposits in the brain are found in amaurotic idiocy Schuller Christian s disease gargoylism and Niemann Pick s disease

Symptoms —The usual classification is into idiots (who are too defective to be able to guard themselves against common physical dangers like falling into the fire) and imbeciles and feeble minded persons (who need to be looked after because of their incapacity to manage their affairs or to profit by instruction) Imbeciles cannot earn their living the feeble minded cannot get on in an ordinary school but may learn a good deal in a special school and be able to earn a living The criterion is in each case mainly a social one the same is true of moral defect', *i e* mental defect coupled with strong vicious or criminal propensities Although these terms are defined in an Act of Parliament they are vague and of administrative rather than medical use An attempt has been made to render them more precise by psycho metric means the customary tests for mental age (usually the Stanford Binet) are applied, and if the subject s intelligence quotient $\left(\frac{\text{mental age}}{\text{actual age}} \times \frac{100}{1}\right)$ be less than 20 he is called an idiot, if it be between 20 and 50 an imbecile if between 50 and 70 feeble minded It must however be recognised that though mental defect is mainly a matter of intellectual capacity it is not solely this and that intelligence tests how ever valuable and trustworthy cannot give a complete indication of the degree of mental defect Even the intellectual defect may be uneven showing much more in some tasks than in others, and it would be a gross error to suppose that a mentally defective person with a mental age of, say $9\frac{1}{2}$ years is mentally in the same state as a normal child aged 9^1 years

The *physical* symptoms are chiefly due to lesions of the central nervous system birth trauma may have led to paralysis spasticity athetosis or there may be evidence of an inflammatory condition of the brain and its membranes as from syphilis The whole clinical picture may be greatly coloured by the motor disturbance *e g* continual rocking and twisting movements grimaces and abnormal posture The special senses may be affected as the result of an independent anomaly *e g* coloboma misshapen ears or from a common cause *e g* interstitial keratitis the retinal changes of amaur otic idiocy It is dubious whether the stigmata of degeneration , such as a Gothic palate or a Darwinian tubercle occur any more frequently among defec tives than in the rest of the population at all events there is none that can be used diagnostically except in the case of mongoloid idiocy There are however some correlations between somatic anomalies and mental defect Thus there are more physical defects among these people than in the average population and this becomes more evident as one looks lower in the scale of mental defect in which skeletal and cardiovascular anomalies may fairly often be found sometimes but not always due to thyroid or pituitary disorders The mongoloid variety is described below

The *mental* symptoms are lack of intelligence and of the normal exercise and control of primitive tendencies This may be extreme as in idiots who cannot be taught to feed themselves and keep clean or who can only just recognise their com panions and make their elementary needs known—they are indeed much less intelli gent than an animal Imbeciles are usually incapable of learning and remembering any but very simple matters They may however be able to do automatically what they cannot understand or put to independent purpose thus idiots savants are especially clever at doing mental arithmetic recalling dates and other such operations What imbeciles manage to learn they cannot utilise in any but the most familiar circumstances Abstract concepts are too hard for them and their judgement is as poor as their grasp or awareness of what is relevant in any situation Though in many

has been standardised on a large adult population it consists of five verbal tests (of comprehension, information digit span forwards and backwards recognition of similarities arithmetical reasoning) and five performance tests (picture completion picture arrangement object assembly, block design digit symbol)

Tests of intelligence are by no means chiefly employed for detecting and measuring defect they have their main field of application in indicating a child s educability and potential attainment and an adult s capacity to undertake certain activities They are used for judging fitness rather than unfitness selecting rather than rejecting It must however be emphasised that intelligence measures cannot be regarded as a measure of height or weight might be they depend on the tests employed, they have varying reliability they cannot be translated into the language and recommendations of practical life unless the interpreter has a clear knowledge of the theoretical and technical limitations implicit in their method To take a self administering' test or a group test of intelligence and to draw merely from the score obtained on it by a child or adult the conclusion that he is mentally defective would be as inept and gross an error as to diagnose active syphilis merely because an unknown laboratory on one occasion reported a positive Wassermann reaction in the patient s blood

There are general observations about mental tests which it is particularly necessary for occasional or inexpert testers to bear in mind The scores must be accurately and as far as possible objectively arrived at therefore the personal opinion of the tester should not enter into them though his skill in administration may have influenced the result Any test which has not been standardised on an appropriate population cannot be safely employed since test scores have no absolute significance they must always be compared with norms and it is imperative that these norms shall have been collected on a suitable group since it would be misleading for example to judge an English child to be less intelligent than an American one because he could not do a test requiring familiarity with American habits and ideas A test to be satisfactory must be both reliable (measuring the subject s ability accurately and consistently) and valid (correlating effectively with other measures of the ability that is being tested) The validation of intelligence tests is a difficult matter sometimes it is carried out by comparing test scores with ratings of intelligence by teachers and other judges or with subsequent educational achievement, and sometimes by the statistical procedure of factorial analysis in which all the items in the test are compared with each other to see whether there is internal consistency

Intelligence tests are different from educational tests They are intended to measure native ability not acquired experience It is true that educational attainment depends largely on innate qualities but the more an intelligence test relies on tasks which demand some acquirement not equally available to all those tested the more misleading may be its results The application of this to verbal tests is obvious a subject who has poor command of English or who has aphasia cannot do himself justice on a test that is satisfactory for the bulk of literate people Performance tests which do not use words are not entirely free from similar defects and in spite of certain merits (greater attractiveness for children tendency to evoke informative temperamental reactions) have conspicuous disadvantages they are seldom cheap or handy, are often inconsistent and unreliable and have poor validity on some of them the subject s performance is much influenced by any emotional or neurotic disturbance he may have Consequently whereas a single predominantly verbal test like the Binet may suffice to indicate the child s or adult s intelligence (provided there is no special verbal difficulty) it would be unsafe to rely on one or even two or three performance tests a median or average score based on half a dozen performance tests is preferable

Group tests have become increasingly popular because they save so much time They are not suitable for testing young children (under the age of 7 or 8) are not so objective and standardised in application as they seem, are by no means foolproof

across the palm) protuberant belly *and low stature* and perhaps a congenital cardiac lesion The similarity in a few respects to juvenile myxœdema and the occasional concurrence of the two conditions sometimes make differential diagnosis difficult not all of the signs here mentioned need be present in any one case On the mental side there is a liveliness and amiability not often seen with so much intellectual defect the patients like music and little jokes of a primitive sort they will imitate gestures but seldom learn to speak properly with their rough harsh voices

The forms of deficiency due to *thyroid insufficiency* and *cerebro macular degeneration* are referred to elsewhere (pp 1483 and 1644) *Epiloia* is the name given to the rare condition in which tuberose sclerosis of the brain, adenoma sebaceum and tumours of the kidney and heart may be associated epilepsy is common and there are gross mental disturbances *Gargoylism* is a rare chondrodystrophy with hepato splenomegaly and mental deficiency In *phenylketonuria* there is increased urinary excretion of phenylpyruvic acid, phenyllactic acid and phenylalanine It is an hereditary disorder due to a single autosomal recessive gene the patients are typically fair haired blue eyed and blonde

Diagnosis —Recognition of gross mental deficiency calls for no skill The degree and kind of impairment however and the somatic variety or cause have to be worked out in every case The latter problem—a minor one except in the case of juvenile myxœdema and syphilis—is to be settled by careful physical examination and enquiry into the history The former is a matter of assessing intelligence and social aptitude

The assessment of intelligence is nowadays a matter of giving the patient tests which have been standardised on average samples of the population What is average or normal at a given age is therefore known and the defective child s performance can be compared with this The most popular and serviceable tests are modifications of those put forward by Binet and Simon in 1908 As these may give a rating that depends unduly on the child s educational opportunities and facility in language and may not indicate special abilities *e g* in mechanical matters many other tests have been worked out which supplement or in certain cases replace the Binet scale A child under the age of 5 cannot be satisfactorily dealt with by the Binet tests which moreover have only limited value for measuring the intelligence of adults It is difficult to agree about what in a normal child must be regarded as the limiting age at which he becomes of adult intelligence it is generally taken as 14 or 16 years In all tests the emotional state of the subject is a factor that may influence his performance The emotional reactions to being tested must be taken along with responses to more familiar situations *e g* at home or at school as evidence of the soundness or instability of the child s personality by such criteria must be judged the social development of the patient his fitness for living in the community or being put under lasting surveillance and control

Mental age and *intelligence quotient* are familiar devices for stating the results of the Binet test and its derivatives In spite of their convenience they are open to so many objections that they might well be dropped now in favour of a percentile scale or one in which test scores are converted into standard scores the statistical properties of which are known The percentile method which requires less familiarity with statistics indicates whereabouts on the curve of distribution a given score comes when a large representative sample of the population is tested Thus whatever the test the score obtained on it can with such a scale permit the conclusion that the person tested falls within say the upper 5 per cent of the population *in this respect* or within the bottom 1 per cent Valuable for children such a method of assessing intelligence (and other qualities) is particularly needed for adults in whom the mental age method is inapplicable Since it has become very plain that it is useful to test the intelligence of adults the inadequacy for this purpose of the Binet scale has led to its being superseded by several tests of which the Bellevue and the Progressive Matrices are probably the best known and most serviceable The Bellevue scale

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depending as they do to some degree on the subject's attitude and situation at the time, about which the group tester will know little or nothing and they cannot be trusted when a low score has been obtained In all instances where a decision must be taken that depends partly on the results of the test any puzzling or unduly low score on a group test should be reinforced by an individual test, such as the Binet or Bellevue It must however be admitted that the inexpert administration of individual tests can yield as rich a crop of wrong conclusions as can the uncritically accepted group test The truth is that ' no mental test score should ever be accepted at its face value nor trusted in the same way as physical measurements are trusted No one ought to use tests who is not willing to familiarise himself with the under lying principles which must be understood if tests are to be applied and interpreted properly and with the literature which bears on the particular tests that he employs In skilled hands testing provides a far surer and more accurate tool for the assessment of abilities than do subjective impressions or the ordinary examination paper But human nature is far too complex to be measured in the simple and direct ways in which physical quantities can be measured and the over enthusiastic but unskilled tester is only too likely to make serious mistakes '

Treatment —PROPHYLACTIC —Eugenic measures are desirable for the rare heredi tary conditions, like amaurotic idiocy, and in the case of those imbeciles and feeble minded in whom genetic rather than environmental causes have been responsible for their maldevelopment and who are capable and desirous of procreating, idiots do not procreate Voluntary sterilisation for eugenic reasons has been recommended by a Departmental Committee but has not yet been explicitly sanctioned by law Birth control, therefore, is the eugenic measure to be advised in cases in which defec tives seem likely to transmit their defect, unfortunately few such defectives can be relied on to observe contraceptive precautions effectively Segregation may indirectly serve the same end Well managed parturition and treatment of parental syphilis are the only other practicable ways of forestalling defect

Educational and social—Much improvement may be attained by the training of defectives it is work for experts Many high grade defectives who would otherwise spend their lives in an institution can be prepared by suitable graduated work under sheltered conditions for an independent life in the general community Where there are special disabilities e g of the senses, or of such capacities as reading and writing attention to these may lift the child out of the class of mental defectives altogether so may education designed to promote emotional stability and self confidence Whether a child lives at home or in a colony or institution will depend not only on the degree of his intellectual and social deficiency but also on the adequacy of his home circumstances There are many kinds of provision for the care of some of the 300 000 defectives in England and Wales ranging from special schools and statutory supervision to mental hospitals an eighth are in certified institutions and a thirtieth more in public assistance institutions Well run colonies providing adequate psycho logical and occupational as well as psychotherapeutic and other clinical services succeed in socialising many defectives hitherto vicious or violent who can then go out and live usefully in the community or in hostels Some, however prove intract able especially those who have epileptic fits

Physical—The bodily disturbances e g contractures and paresis call for ortho pædic treatment which sometimes benefits the mental state The treatment of the forms due to thyroid deficiency or syphilis is described elsewhere

AUBREY LEWIS

APPENDIX

HISTOPLASMOSIS

Definition —An acute subacute or chronic infection of man and certain animals by the fungus *Histoplasma capsulatum* giving rise to three main clinical types of disease (i) the disseminated form where the parasites invade the reticulo endothelial cells in many parts of the body (ii) the primary pulmonary form confined to the lungs and adjacent lymph nodes (iii) a localised infection of the skin or the mucous membranes of the mouth tongue or pharynx

Ætiology —The fungus exists in two forms (i) a mycelial phase which is found when it is existing as a saprophyte or if it is cultured at a temperature of 22 C (ii) a yeast like phase which occurs when it is living as a parasite or if it is grown on enriched media at 37 C Infection from natural sources is probably due to the mycelial phase but it is the yeast like phase that is parasitic and invades the tissue cells change from one form to the other readily occurs

The fungus has been isolated from the soil in many areas and some twenty species of animal have been found to harbour the parasite the bulk of natural infections being found in dogs cats and rats it has also been found in a high proportion of skunks and opossums but only small numbers of these animals have been examined Birds have not been found infected with *Histoplasma* and seem to be highly resistant to it though the fungus can be found in profusion in their droppings and in the litter of poultry houses A number of small epidemics have occurred on farms in the United States and amongst builders working in lofts where birds roost, caused probably by inhalation of infected dust The adoption of the deep litter method of poultry farming in this country suggests the possibility of similar outbreaks arising particularly in the more humid western counties Both sexes are susceptible at all ages the highest incidence being either during the first year of life or in the later adult years Amongst adults males are infected seven times as frequently as females

The chief portal of entry is thought to be the respiratory tract but the dissemin ated form may originate in some part of the gastro intestinal canal Primary skin lesions also occur but they are uncommon Special precautions seem necessary in laboratories as already 41 cases of infection with clinical illness have been reported amongst laboratory workers who had been handling *H capsulatum* The incubation period is not known with certainty but is thought usually to be from 4 to 6 weeks with a range of from 2 weeks to 3 months *H capsulatum* has a world wide distribution although clinical cases occur somewhat sporadically outside North America In Great Britain at least 15 cases have been diagnosed with certainty but it is thought that in the majority the infection was acquired elsewhere The principal endemic centre is in the United States of America where the greatest incidence is found in an area extending from the Great Lakes to the Gulf of Mexico in the valleys of Ohio Missouri Arkansas and Mississippi rivers

Pathology —The fungus invades and multiplies within the reticulo endothelial cells and in the disseminated form it may be found throughout the body or confined to a single organ the suprarenal glands often being the principal or only organ involved In acute disseminated infections with a fatal termination intra cellular organisms may usually be found post mortem in stained sections of tissue from the lung liver spleen and suprarenal glands The gastro intestinal tract is often affected and the bone marrow almost invariably The organism produces greyish white nodules usually multiple varying in diameter from 2 to 3 mm up to several centi metres Extensive areas of necrosis may be found surrounded by granulomatous

organism is found most easily in smears obtained by sternal or splenic puncture but may also be seen in smears from the lesions where these are accessible and at times in the cytoplasm of the mononuclear blood cells Very occasionally in heavy infections a direct sputum smear will show the organism

Culture—If the infection is scanty culture will be necessary and this is the method for definitive diagnosis Cultures should be made on enriched blood agar to which small quantities of penicillin and streptomycin have been added Infected material such as blood bone marrow or sputum should be rubbed over the culture medium the plates then being closely sealed with cellophane tape It is essential to incubate some of the plates at room temperature as at 37 C only yeast like bodies are produced At room temperature an abundant aerial mycelium is formed consisting of septate hyphæ with numerous microconidia attached to their sides or growing on short lateral branches In addition there are the rounded tuberculate chlamydospores which are characteristic of *H capsulatum* and their presence makes diagnosis conclusive The material used for culture must be fresh and the cultures should be observed for 6 to 8 weeks before they may be considered negative

Histoplasmin Skin Reaction—The histoplasmin skin reaction develops within a few weeks of infection 0 1 ml of a 1 1000 dilution of standardised histoplasmin is injected intracutaneously The reaction is read after 48 to 72 hours in the same way as for the tuberculin test A positive reaction is found not only during the clinical stage of the disease but in many healthy persons living in endemic areas As such reactors have an unusually high incidence of pulmonary calcification it seems probable that a past infection with *Histoplasma* has healed spontaneously without causing any recognisable illness

Complement Fixation Test—In acute infections complement fixing bodies appear in the blood towards the end of the third week of the illness and increase during its course gradually diminishing as recovery sets in In chronic pulmonary infections they may persist at a high level for many years The complement fixation test is a valuable aid to diagnosis and should be employed whenever infection by *H capsulatum* is suspected The test may become negative in the terminal phase of the disseminated form of the disease but the fungus can then usually be identified readily by blood or bone marrow culture or by the examination of tissues obtained after biopsy has been performed The antibodies produced cross with the antigens of other fungi particularly *coccidioides immitis* and *blastomyces dermatitidis* These cross reactions do not however invalidate the complement fixation test as the titres of the homologous antigen are significantly higher

When biopsy is possible sections of enlarged lymph nodes or of tissues from superficial lesions may show endothelial cells packed with *H capsulatum* Caution is necessary however when considering biopsy since two recent case histories have revealed that shortly after a biopsy was performed each patient having been previously in good health generalised symptoms typical of the disseminated form of histoplasmosis arose followed by death a few months later The diagnosis was confirmed post mortem and it appears possible that the organism was disseminated into the blood stream when the biopsy was performed

Prognosis—In the past histoplasmosis was often considered to be an almost invariably fatal disease More recent knowledge indicates that the mortality is probably extremely low since it is considered reasonable to assume that a positive histoplasmin skin test indicates past invasion of the tissues of some part of the body by the fungus and such positive reactions have been obtained from several millions of persons in the United States Such persons often have scattered calcified areas in the lungs such as are found after histoplasmosis It is thought therefore that the majority of infections are overcome without any noticeable disturbance of health or the disease passes unrecognised as the illness is of short duration and spontaneous recovery ensues

Where the diagnosis is made during the clinical course of the disease it may be

tissue Superficial or deep ulcers may be seen in the small or large intestine and nodules have been found in the submucosa and deeper layers of the intestinal wall Caseation of the suprarenal glands may cause almost total destruction of glandular tissue, and a recent review of 103 fatal cases of histoplasmosis revealed that 35 per cent were found post mortem to have some damage to suprarenal glands Infections commencing in the mouth pharynx or larynx show localised necrotic ulcerations and enlargement of the regional lymph nodes

In the benign pulmonary infections multiple small discrete, fibrotic nodules may be found in any part of the lungs and early enlargement of the tracheo bronchial and hilar lymphatic glands is usual The central portions of the nodules become caseous and later calcify these residual lesions are often seen in a routine radiograph taken months or years after the infection occurred When the lung is involved in the disseminated form of the disease there is usually an extensive bilateral inter stitial pneumonitis in the early stage of the illness with diffuse or localised areas of consolidation At times abscess formation occurs which may be followed by cavita tion Where healing takes place fibrosis with contraction often causes deformity of a section or lobe, and a clinical diagnosis of chronic tuberculosis or bronchiectasis is not an uncommon error where it occurs near the lung roots it may be mistaken for a bronchogenic carcinoma Occasionally the infection is confined to the medi astinal lymph nodes and a picture almost indistinguishable from Boeck s sarcoid or lymphoma is presented

Clinical Features —(i) *Disseminated histoplasmosis* —This may be an acute and rapidly fatal illness and this form is most common in infants, in the aged or in those debilitated by tuberculosis or malignant disease More commonly it runs a sub acute course the illness extending over many months with a fatal termination in most instances although arrest of the disease and ultimate recovery have been recorded a number of times

There is no characteristic clinical picture Common early features are debility, loss of weight low grade fever sweating joint and muscle pains abdominal dis comfort and diarrhœa Leucopenia and progressive anæmia are almost invariable and enlargement of the liver and spleen are usually found Involvement of the suprarenal glands may destroy so much glandular tissue that Addison s disease results and histoplasmosis should always be excluded when such a diagnosis is made If the infection spreads to the lung it will usually give rise to a pneumonitis with an abrupt onset accompanied by fever around 103 to 104° F but seldom any clinical features to distinguish it from a viral pneumonia Symptoms may be limited to occasional chest pain and a dry unproductive cough The physical signs are seldom of any diagnostic value By contrast a radiograph shows an extensive bilateral inter stitial pneumonitis miliary or patchy together with enlarged hilar lymph nodes The acute stage lasts for 7 to 10 days followed by gradual subsidence The radio graphic signs however do not reach their maximum for 2 weeks after 6 weeks a fine nodular fibrosis may be seen and after 3 months nothing abnormal may be detected More often though, when recovery takes place contraction follows the fibrosis with marked deformity of the affected lung section

(ii) *Primary pulmonary histoplasmosis* —This form is very often asymptomatic it may cause mild catarrhal symptoms and malaise and suggest influenza or bronchitis Spontaneous recovery is the rule and the disease is seldom recognised before this has taken place It may be months or years before the residual lesions are seen in a radiograph as the examination is nearly always made either as a routine or for some other condition

Laboratory Findings —The fungus may usually be found in the cytoplasm of the reticulo endothelial cells and in the macrophage cells in the form of round or oval yeast like bodies varying from 2μ to 4μ in diameter Smears stained by Giemsa s method show chromatin irregularly condensed within a refractile capsule The

TOXOPLASMOSIS

Definition —An uncommon disease of man and animals of world wide distribution caused by a small protozoon *Toxoplasma gondii* which may be transmitted to the foetus *in utero* by an infected mother or acquired by some means as yet unknown in childhood or in adult life The majority of infections probably pass unnoticed but the parasite may give rise to a wide variety of symptoms and signs of differing severity and variable duration depending partly upon the age of the person when infected which tend to be so grouped that four main clinical types of illness may be recognised

1 CONGENITAL —This form is characterised by encephalomyelitis cerebral calcification hydrocephalus and choroidoretinitis with symptoms either apparent at birth or appearing soon afterwards

2 ACQUIRED —

(i) *Cerebrospinal*—most frequent in children in whom the most typical manifestations are those of an acute meningoencephalitis

(ii) *Lymphatic*—characterised by the enlargement of one or more groups of lymphatic glands with at times fever of several weeks duration and marked constitutional disturbance

(iii) *Exanthematous*—the form most frequently found in adults presenting as an acute febrile illness with a widespread maculo papular rash a diffuse interstitial pneumonitis myocarditis and at times meningoencephalitis

(iv) *Latent*—where infection by *T gondii* gives rise to no symptoms or signs of the disease and diagnosis can only be made by means of laboratory tests Latent infections are found only in adults and are probably always acquired after the age of childhood

Ætiology —The causal organism was first discovered in 1908 in a small North African rodent the gondi (*ctenodactylus gundi*) and it was named *Toxoplasma gondii* Nicolle and Manceaux It was thought to be a protozoon and was classified as one of the sporozoa but there is still much doubt about its true position Although many species have since been described *T gondii* is considered the only species occurring in man and animals all other forms described being considered strains of a single species since both morphologically and immunologically they all appear to be identical

T gondii is an intracellular parasite found usually in the endothelial cells the mononuclear leucocytes or the tissue cells Free living forms may also be found in the tissue fluids of the host In this free extracellular form the parasite is a slender crescent shaped organism with one end rounded and the other pointed measuring from 4μ to 6μ in length its breadth being around 2μ Intracellular forms often lose the crescent shape becoming pear shaped oval or rounded when they may readily be confused with *Leishmania* In dry films stained by Wright s or Giemsa s methods the cytoplasm is blue the granular nucleus which is single and fills about one quarter of the cell stains a reddish purple and will be seen near the rounded extremity whilst towards the pointed end there is a small deeply staining red granule the paranuclear body The parasite multiplies by longitudinal fission within the endothelial and tissue cells of its host With virulent strains these cells rupture early releasing the parasites which then invade fresh cells thus enabling the parasite to multiply extremely rapidly though in the light of present knowledge with doubtful benefit to itself since it may result in an overwhelming and rapidly fatal infection of its host With less virulent strains the cells often remain intact allowing reproduction to continue until they become greatly distended by 80 or more parasites

said that in primary pulmonary histoplasmosis, recovery nearly always occurs spontaneously and the prognosis is excellent Localised infections are more serious and run a much more prolonged course They usually progress by localised extension, and unless the disease is arrested they tend to be ultimately fatal There are, however a number of records where the disease has continued for many years without any serious disturbance of health to the persons affected

More than one quarter of the fatal illnesses occur in infants under 1 year of age In these the disease is nearly always in the disseminated form, and up to the present time it has been found that over two thirds of all cases of disseminated histoplasmosis have a fatal termination

Treatment—It is fortunate that the great majority of cases recover unaided since despite favourable initial reports on a number of new compounds there is not yet sufficient evidence to consider any of them curative

Most of the established antibiotics and sulphonamides have been tried and they have all been reported to be ineffective although recent laboratory trials have shown that several sulphonamide compounds do have a pronounced action on *Histoplasma* and are capable of overcoming infections in mice previously innoculated with lethal doses of *H capsulatum* Sulphanilyl thiourea is by far the most active of the many compounds tested possibly because unlike most of the other sulphonamides it is only partially inactivated by *p* aminobenzoic acid The yeast phase of the fungus is far more sensitive to the drug than is the mycelial phase and this may explain its efficacy in histoplasmosis in mice which is usually a very acute and rapidly fatal infection In the more chronic infections, common in humans the mycelial phase of the fungus may predominate, making its eradication much more difficult Further clinical trials of sulphonamides seem necessary

The use of cortisone and related compounds should be avoided in histoplasmosis as it has been found that the initial improvement that often occurs following their administration is temporary and rapid extension of the disease often follows When the suprarenal glands have sustained such severe damage that Addisonian crises occur cortisone will be necessary to tide over the crisis and to prevent their recurrence small maintenance doses together possibly with DOCA should be given

Ethyl vanillate received favourable reports when first used but later trials failed to confirm its value Stilbamidine and more recently 2 hydroxy stilbamidine have been used, and they have appeared to have a favourable influence upon the course of the disease although the response to their administration is somewhat uncertain

Two drugs still undergoing laboratory trials have given encouraging results combining powerful anti fungal properties with low toxicity for many different species of animal One nystatin (fungicidin) is an antibiotic which has been marketed under the trade name of Mycostatin In laboratory animals it has proved to be highly effective in all forms of infection whether fulminating moderately acute or chronic and the therapeutic doses have not been toxic In contradistinction to sulphanilyl thiourea nystatin is more active against the mycelial phase of *H capsulatum* If the preliminary reports on these two drugs are substantiated treatment with a combination of the two may prove to be highly effective

The other drug MRD 112 (β diethylaminoethyl fencholate) also has marked anti fungal properties combined with a low toxicity In human infections it has been given by intravenous injection commencing with a dose of 50 mg daily later increased to 150 mg daily the duration of treatment being 24 to 28 days The higher dose may cause drowsiness at first but clinical improvement has been apparent soon after the commencement of treatment although radiographic studies have shown very little change in the lungs throughout this period It should however be remembered that in cases with an acute pneumonitis due to histoplasmosis the radiographic signs in the lung do not usually reach their maximum for 2 to 3 weeks after the onset although subsidence of the infection often commences after 7 to 10 days

it Neither is it always easy to reproduce the disease in animals and it has been found that if dogs are inoculated with the parasite even with highly virulent strains only the younger pups develop the acute form of the disease the older dogs remaining quite free from all signs of infection Recently dogs have been suggested as a probable source of human infection as not only has acute toxoplasmosis occurred in the owners of dogs harbouring *T gondii* but neutralising antibodies have been demonstrated in the blood of more than one third of the owners of dogs from whom the parasite has been recovered Whatever significance may be attached to such findings it should be remembered that as there is usually a very close association between dogs and their owners it is equally probable that both could have been infected simultaneously from the same source

Until the life cycle of *T gondii* is known it seems unlikely that the many problems concerning the epidemiology of toxoplasmosis will be solved Of the many prevailing surmises on the mode of entry of the parasite into the human body the majority of those who have studied the disease consider the three following routes the most probable

(i) the gastro intestinal tract following the ingestion of infected food
(ii) the respiratory tract by inhalation of droplets containing the parasite
(iii) the skin and blood stream following the bite of an infected arthropod

It is not yet known whether the vegetative forms of *Toxoplasma* are as vulnerable to human gastric juice as they are to that of experimental animals nor is it known how resistant the pseudocysts are to storage desiccation cold or heat Since they occur quite frequently in the muscles of animals used as food the eating of raw or insufficiently cooked meat would seem a likely source of infection The pseudocysts have also been found in the ovaries of hens it is therefore possible that eggs could convey the infection Recently toxoplasmosis has been recognised in cattle and the disease has been transmitted to calves both congenitally and in the milk In nearly all rural areas in Great Britain unpasteurised milk is the only form available and this could well provide another source of infection should the disease become common in cattle

It has already been mentioned that *Toxoplasma* are present in the bronchioles and probably in the sputum of human cases of toxoplasmosis with pneumonitis and this is true of domestic animals with clinical evidence of the disease Moreover respiratory symptoms are a much more prominent feature of the disease in most animals than they are in man and thus those looking after such sick animals might well become infected by the inhalation of infected droplets and also possibly through the con junctiva since animals have been infected by this route

Apart from the bites of infected insects infection *via* the skin is also possible through the handling of infected tissues as it is known that *Toxoplasma* can penetrate closely shaved skin and it is therefore not improbable that some human infections may be caused by the parasite entering through cracks and small abrasions in the skin This would certainly explain the increased proportion of positive serological reactions that has already been observed in veterinary surgeons slaughterhouse workers and in particular in those handling rabbits

Pathology—Following infection the parasites are distributed throughout the body by the blood stream and become established in the cells of the reticulo endothelial system and also in the parenchymal cells Localisation occurs in many organs more often in the brain lung liver or spleen parasites often being found also in the kidney suprarenal glands bone marrow and lymph nodes Muscle fibres are also invaded in particular those of the heart as well as the skeletal muscles They may also be found within phagocytic cells and living free in the intracellular fluids of the affected organs

The typical lesions are small focal areas of necrosis surrounded by a zone of

their nuclei are then extruded, and the hypertrophied cyst like structures that remain packed with parasites are known as pseudocysts Within them the parasites seem to be in a resting or inactive stage, causing little tissue damage or cellular reaction the cyst wall probably affording protection from any circulating antibodies thereby enabling a chronic infection to become established

T gondii can be cultivated in the laboratory if living tissue cells are used It propagates most readily on the chorio allantoic membrane of the developing chick embryo at 35° to 37 C if protected from bacterial contamination and dehydration The embryo usually dies between the seventh and tenth days

Epidemiology —*Toxoplasma gondii* has been found in many species of mammals and birds and also in certain reptiles The first authenticated report of human infection was made in 1923 since when human infections have been recorded in many European countries, including Great Britain in the Middle East Ceylon North Central and South America, Australia and Hawaii The incidence of toxoplasmosis in man is not known yet, but subclinical infections are probably much more frequent than it is generally realised Recent surveys using serological tests have shown that positive reactions, suggesting a past infection may be given by from 10 to 50 per cent of the adult population in many areas Such figures should however be treated with caution since doubt has been cast on the validity of some of the tests used it having been found that they are not specific for *T gondii*

Very little is known about the transmission of the parasite to humans or of the source whence it originates, though it is thought to be conveyed from animal reservoirs by some means still awaiting discovery Rodents and dogs in particular are thought to be a possible source of infection

Neonatal infections appear to be conveyed transplacentally to the fœtus from an infected mother who almost invariably remains free from any symptoms of the disease herself If the infection is acquired early in pregnancy by the mother, abortion will probably result or if the pregnancy continues the fœtus will be so extensively damaged that it will be stillborn Infection late in pregnancy may result in the infant being free from any signs of the disease at birth and several weeks or even 2 or 3 months may elapse before signs and symptoms appear Later offspring from such mothers with one possible exception have never yet been born with toxoplasmosis It seems probable that if the mother became infected during the puerperium the disease could be transmitted to the infant if it was breast fed, as lactating laboratory mice have conveyed the parasite to their offspring in the milk

Laboratory workers handling *Toxoplasma* have several times acquired very severe or fatal infections though by what means remains unknown

Direct case to case infection seems improbable since laboratory animals have hardly ever been known to infect their cage mates even in experimental conditions planned to achieve it In the adult form of the disease with a diffuse pneumonitis the parasites are often plentiful in the secretions in the small bronchioles and in such cases droplet infection would seem a possibility

Nearly all warm blooded species of animals can be infected experimentally and the parasite has been transmitted in the laboratory

(i) by feeding to animals either tissues containing it or food contaminated with fæces in which it is present
(ii) by inoculation by almost any of the usual routes intranasal intravenous intraperitoneal intracerebral or subcutaneous
(iii) by direct penetration of closely shaved skin by the parasite,
(iv) by penetration of the mucous membrane of the vagina and the conjunctiva

Infection of animals by the alimentary route is not always easy as the gastric juice tends to kill the vegetative forms of *Toxoplasma* The pseudocysts are more resistant and the feeding of tissues containing them has proved to be the easiest way of achieving

The signs secondary to encephalomyelitis most frequently found are muscular twitchings and convulsions stiffness of the neck paraplegia respiratory weakness and cyanosis which at times may be due to an interstitial pneumonitis vomiting and diarrhœa Hydrocephalus develops in the majority of infected infants and rapid enlargement of the head may occur At times when there is early and extensive cerebral damage microcephaly may be found The cerebral lesions become calcified if the infant survives long enough and may later give rise to Jacksonian convulsions and the majority of infants who survive for a number of years are nearly always mentally deficient

The ocular findings most frequently include microphthalmia, the small eyes being in striking contrast to the enlarged head nystagmus which may result either from poor fixation due to choroidoretinitis or from the lesions in the central nervous system vitreous opacities and choroidoretinitis The lesions are nearly always bilateral and cause blindness or very severe impairment of vision in those infants who survive The majority of infants however die within the first few weeks of life

2 ACQUIRED TOXOPLASMOSIS

(i) *Cerebrospinal*—In the earlier accounts of toxoplasmosis this form of the disease was usually considered to be not only the invariable manifestation of infection in children but also to be confined solely to them Meningo encephalitis has in recent years been reported many times in adults with the disease but it is seldom the initial feature of the attack usually occurring as a complication of the exanthematous form towards the end of the first or second week of the illness not infrequently after the acute stage has subsided and recovery appears to have commenced

The cerebrospinal form is probably still found more frequently in children in whom it tends to be the predominant feature of the illness The onset is marked by fever very severe headache vomiting and delirium Convulsions often occur a day or two later and the picture presented may suggest a brain tumour Deafness is often found and very occasionally choroidoretinitis has been recorded but it is not a constant feature as in the congenital infections The attacks are frequently severe and often rapidly fatal with death following within a few days of the onset Some infections run a more chronic course but not necessarily with a more favourable outcome since death may occur several weeks after the commencement of the illness Complete recovery is however by no means uncommon without the development of any sequelæ even when the attack has been exceedingly severe

(ii) *Lymphatic*—Some of the earlier accounts of toxoplasmosis mentioned that a generalised enlargement of lymphatic glands was occasionally observed but it is only in recent years that the lymphatic form has been recognised as a clinical type that occurs without any of the other manifestations of the disease It has been stated quite recently that probably the commonest manifestation of acquired toxoplasmosis in man yet known is a lymphadenitis resembling glandular fever The total number of cases of this form of infection reported to date does not yet seem large enough to confirm the above statement Although the lymphatic form is not usually described as occurring predominantly in children nearly all the recorded cases have been found between the ages of 5 and 15 years

As with most infectious illnesses there is a fairly wide range in the severity of the attack and there seems to be no practical advantage in adopting the classification which divides this form into three main clinical groups since they do not appear to differ except in severity

A proportion of these cases have a sudden febrile onset often with a rigor and fatigue is a common premonitory symptom which precedes the onset by several days The fever usually rises rapidly to about 104 F and is frequently accompanied by catarrhal symptoms cough headache and pain in the back At times the throat is

inflammation containing lymphocytes mononuclear and plasma cells Hypertrophied cells distended with parasites the so called pseudocysts are often seen Serous exudates are commonly found in the various body cavities

In congenital cases lesions predominate in the brain, spinal cord, retina and choroid Inflammation often extends to the ependyma causing ventricular block and hydrocephalus As well as the typical necrotic foci minute granulomata are also found in the brain which calcify if the affected infant survives long enough The lesions in the central nervous system are not very marked and often sections must be searched with the greatest diligence before they are seen.

In the acquired adult infections which usually pass unnoticed the lesions are often found accidentally Rarely there is a widespread dissemination of the parasite with lesions throughout the body though more often the predominant feature is an interstitial pneumonitis with thickening of the alveolar walls and infiltrations of giant and plasma cells There may also be scattered areas of purulent bronchiolitis Inflammatory and necrotic areas are also quite frequently found in the liver, spleen and heart muscle and encephalitis has occurred in several adult cases, though it is seldom as predominant a feature as in congenital infections or in the acquired infections of children

Clinical Features —As knowledge of toxoplasmosis increases and as more clinical reports become available so does it appear that the sharply demarcated clinical syndromes that were described in the earlier accounts of the disease do not in reality exist apart from the fairly clear cut distinction between congenital and acquired infections

Whilst it is still true that there is a preponderance of certain clinical features in children suffering from toxoplasmosis, with others appearing with greater frequency in adults, there no longer seem to be any clinical manifestations of acquired toxoplasmosis that are sufficiently exclusive to one or other age group to justify the old subdivision into acquired infections—in children, and acquired infections in adults

I CONGENITAL TOXOPLASMOSIS

Acute infections with widespread dissemination of the parasites and necrotic lesions in many organs in particular the lungs, the heart liver spleen kidney supra renal glands and lymphatic glands have been described but occur very infrequently in congenital toxoplasmosis Subacute infection is the common form, with predominating neurological symptoms which may be noted at birth or shortly afterwards If the fœtus is infected very early in pregnancy the disease will reach an advanced stage *in utero* and cases have been recorded where the pregnancy having continued to term was followed by an obstructed labour owing to the development of hydrocephalus in the fœtus

In the typical subacute congenital infection the symptoms and signs may be subdivided into

(i) those due to the presence of parasites within the body these may be called primary symptoms and signs
(ii) those secondary to the principal lesions caused by the parasite namely encephalomyelitis and choroidoretinitis

The common primary signs are fever with a fluctuating temperature which may at times be subnormal jaundice which has been described in about one third of all congenital cases purpura which occurs infrequently and a maculo papular rash which is extremely rare Anæmia and leucocytosis with an absolute increase in monocytes and lymphocytes, are found in about one half of all cases and the liver and spleen are not infrequently enlarged

much more constant In several proved cases eosinophils have been raised to from 14 to 20 per cent of the differential count

(ii) *Cerebrospinal fluid* —This is often xanthochromic in cases with encephalo myelitis Protein usually considerably increased, the increase being relatively greater than that of the cells Sugar normal in amount or slightly decreased Cells leucocytes are often present in large numbers with a very considerable range an average or usual figure being around 500 per c mm though counts of 60 and 1600 are often recorded erythrocytes are usually present but in lesser numbers

Definitive Diagnosis —The definitive diagnosis of toxoplasmosis by the direct isolation of *T gondii* from the patient is frequently not possible and therefore in direct methods are also employed and provided that a full range of investigations is carried out with consistent findings a diagnosis of toxoplasmosis may still be established with reasonable certainty

(i) *Morphological Identification of Toxoplasma* —During the acute stage of the infection the parasite may sometimes be found in stained smears of bone marrow in material obtained by splenic puncture or in the centrifuged deposits of exudates cerebrospinal and ventricular fluids Fresh cover slip preparations should also be examined Smears should likewise be made from a portion of any tissues removed at biopsy or autopsy and these should be stained with Giemsa the other portions should be fixed and thin sections made which should be stained with hæmatoxylin and eosin and then very carefully examined with an oil immersion lens The para sites in the pseudocyst form are those most easily recognised after a little experience

(ii) *Biological Identification of Toxoplasma* —Material obtained from a suspected case of toxoplasmosis should be inoculated into laboratory animals which must be free from naturally occurring infection in themselves Mice hamsters and guinea pigs are the most satisfactory animals and at least six mice and two guinea pigs must be used before any reliance can be placed on the test Similar material to that used for making stained smears should be injected intracerebrally into the mice and intra peritoneally into the guinea pigs The animals should be watched for signs of illness if after a month all have remained well, passage to another group of animals should be undertaken by the inoculation of tissues from one half of the first group Where illness develops exudates should be carefully examined and if *Toxoplasma* are not found part of these fluids should be inoculated into other animals Smears should be made and carefully examined from the brain lung liver spleen and the peritoneal lining of any animals that die The parasite may be found after the primary inocula tion and it is frequently isolated after the first passage For practical purposes not more than three passages should be performed since it is quite exceptional for the parasite to be recovered if the first three passages have proved to be fruitless

Direct demonstration of the parasites has only been possible in about one half of the total number of human cases so far described

Indirect Methods of Diagnosis —(i) *Complement Fixation Test* —An antigen derived from chick embryo cultures should be employed and the test serum should be exam ined within 24 hours of taking the blood as complement fixing activity may develop spontaneously after a longer period Complement fixing antibodies develop 3 to 4 weeks after infection occurs and may persist for several years in fairly high titre although they often disappear during convalescence Some 10 per cent of healthy adults give a positive result with this test but a titre of over 1 8 suggests a recent infection

(ii) *Neutralising Antibody Test* —Infection with *T gondii* leads to the formation of antibodies in the blood which may persist for many years after recovery They may be demonstrated by their ability to prevent infection of the chick embryo with *Toxoplasma* or the development of skin reactions in the rabbit Although all human

sore and there may be abdominal discomfort and diarrhœa These symptoms and the fever nearly always precede the glandular enlargement and it may be a week or more before the enlarged glands are first observed The fever usually last for 2 to 3 weeks occasionally for a few days only whilst it has at times in adult infections been pro longed for 6 to 7 weeks with a high initial fever of about 105° F, slowly subsiding to about 102° F some ten days from the onset after which it may fluctuate between 100° F and 101° F for 2 to 3 weeks before slowly returning to normal Although there are no complications and recovery invariably follows the febrile cases often require a prolonged convalescence, fatigue being a very prominent feature for 3 or 4 months following an attack

A large number of cases are afebrile and free from any symptoms apart from at times some initial tenderness in the region of the enlarged glands the general health remains unaffected by the infection Others remain unaware even of the enlarged glands which are found during some routine examination

The characteristic feature of this form of toxoplasmosis whatever degree of severity it may assume is enlargement of one or more groups of lymphatic glands Those most frequently affected are the cervical suboccipital axillary and inguinal groups A radiograph of the chest may also reveal enlargement of the hilar glands Enlargement of the cervical glands is fairly constant and they are nearly always the first glands to become affected other groups becoming enlarged after an interval of several days or even 1 to 2 weeks The glands are usually firm discrete and vary in size from that of a hazelnut to that of a walnut They are usually painless though there may be some initial tenderness during the first week or two of the illness There is no inflammation of the skin overlying the glands and suppuration does not occur

Another very characteristic feature of all cases whether febrile or afebrile is the persistence of the glandular enlargement enlarged lymph nodes usually can be found 6 to 9 months after the onset of the attack

(*iii*) *Exanthematous* —Although many clinical forms have been described in adults the most typical is an acute febrile illness of sudden onset sometimes marked by rigors soon followed by the appearance of a generalised maculo papular rash which is absent from the palms of the hands and the soles of the feet and which closely re sembles the rash of typhus or Rocky Mountain spotted fever There may be a disseminated myositis giving rise to severe aching pain in the muscles or at times to myocarditis when the heart muscle is involved The outstanding feature however is a diffuse interstitial pneumonitis resembling an atypical virus pneumonia which frequently runs a rapid course with severe dyspnœa cyanosis and respiratory failure Enlargement of the liver and spleen will be found in a few cases and encephalitis has recently been a feature of several acute cases in adults

Diagnosis —*Clinical Diagnosis* —Even presumptive evidence of *Toxoplasma* infec tion is rarely obtainable on clinical findings alone except in infants A combination of convulsions hydrocephalus or microcephaly choroidoretinitis and calcified areas in the brain seen in a radiograph strongly suggests toxoplasmosis when found in infancy and in older children a similar picture together with blindness or serious impairment of vision and mental deficiency makes a similar diagnosis equally prob able In adults clinical diagnosis is extremely difficult and it is more likely to be considered under the differential diagnosis of an unidentified infection than as a probable diagnosis by itself

Laboratory findings —The usual routine laboratory investigations give little help in toxoplasmosis (i) *Blood* —Anæmia of moderate degree is usual particularly in infants though the hæmoglobin is seldom less than 12 3 g or the red cell count below 4 million The leucocytes are usually slightly increased in numbers from 9000 to 12 000 being a common finding with a considerable increase in lymphocytes and monocytes in many cases the increase in monocytes being of lesser degree but

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limited to a few reports but it appears to be the most effective remedy at present available particularly when combined with sulphadiazine The effect of this combination appears to be synergistic since it has been found to be six times greater than would be expected if it was purely additive The best results are given by a combination of 22 per cent pyrimethamine to 78 per cent sulphadiazine The most effective doses of pyrimethamine are considerably higher than those normally used in practice the lower dosage being adopted on account of the risk of toxic effects Treatment is usually commenced with a small dose of 25 mg daily which is increased after 3 or 4 days to 50 mg daily Treatment is usually continued for 10 to 14 days the total dosage of pyrimethamine being from 500 to 700 mg In one series of 13 cases receiving this treatment one patient was left with a psychosis the cause being unknown complete recovery was recorded for the remainder Pyrimethamine has also been tried in cases of uveitis where serological tests suggested toxoplasmosis to be a possible cause The results so far have been rather indecisive but further trials are still in progress